## WEBVTT

NOTE duration: "00:57:10.3790000"

NOTE language:en-us

NOTE Confidence: 0.7699789

 $00:00:00.000 \longrightarrow 00:00:02.170$  Rounds we have two speakers

NOTE Confidence: 0.7699789

00:00:02.170 --> 00:00:04.340 today from male to wonderful

NOTE Confidence: 0.7699789

00:00:04.422 --> 00:00:07.054 speakers first or Hegel on my own,

NOTE Confidence: 0.7699789

 $00{:}07.060 \dashrightarrow 00{:}00{:}09.538$  introduced and then the cold diesel,

NOTE Confidence: 0.7699789

 $00:00:09.540 \dashrightarrow 00:00:12.330$  who Linda Irwin will introduce.

NOTE Confidence: 0.7699789

 $00:00:12.330 \longrightarrow 00:00:13.795$  I've known Jorge since

NOTE Confidence: 0.7699789

 $00:00:13.795 \longrightarrow 00:00:15.620$  before he arrived at Yale.

NOTE Confidence: 0.7699789

00:00:15.620 --> 00:00:17.816 He's now the Lucille P Marquis,

NOTE Confidence: 0.7699789

 $00{:}00{:}17.820 \dashrightarrow 00{:}00{:}19.221$  professor, microbial pathogenesis

NOTE Confidence: 0.7699789

 $00:00:19.221 \longrightarrow 00:00:21.556$  and chair of the Department.

NOTE Confidence: 0.7699789

 $00:00:21.560 \longrightarrow 00:00:23.680$  In his lab studies bacterial infections,

NOTE Confidence: 0.7699789

00:00:23.680 --> 00:00:25.810 he's probably best known for his

NOTE Confidence: 0.7699789

 $00:00:25.810 \longrightarrow 00:00:27.224$  discovery and characterization of

NOTE Confidence: 0.7699789

 $00{:}00{:}27.224 \dashrightarrow 00{:}00{:}28.989$  the Type 3 secretion apparatus,

 $00:00:28.990 \longrightarrow 00:00:30.760$  which is this microscopic needle

NOTE Confidence: 0.7699789

 $00:00:30.760 \longrightarrow 00:00:32.529$  that injects proteins into cells.

NOTE Confidence: 0.7699789

 $00:00:32.530 \longrightarrow 00:00:33.592$  A fantastic story,

NOTE Confidence: 0.7699789

 $00:00:33.592 \longrightarrow 00:00:35.720$  and in recognition of this work,

NOTE Confidence: 0.7699789

 $00:00:35.720 \longrightarrow 00:00:37.838$  he's received numerous awards and been

NOTE Confidence: 0.7699789

00:00:37.838 --> 00:00:40.318 elected to the National Academy of Sciences,

NOTE Confidence: 0.7699789

 $00:00:40.318 \longrightarrow 00:00:42.796$  but more recently he's got interested in

NOTE Confidence: 0.7699789

 $00:00:42.800 \longrightarrow 00:00:44.922$  the Association between cancer and bacteria,

NOTE Confidence: 0.7699789

00:00:44.922 --> 00:00:47.046 and mechanistically, how does that work,

NOTE Confidence: 0.7699789

 $00:00:47.046 \longrightarrow 00:00:48.820$  and he's shown, for example,

NOTE Confidence: 0.7699789

 $00:00:48.820 \longrightarrow 00:00:50.589$  that some bacterial toxins can

NOTE Confidence: 0.7699789

00:00:50.590 --> 00:00:51.748 induce DNA damage.

NOTE Confidence: 0.7699789

 $00{:}00{:}51.748 \dashrightarrow 00{:}00{:}53.542$  And therefore are potential carcinogens.

NOTE Confidence: 0.7699789

 $00{:}00{:}53.542 \dashrightarrow 00{:}00{:}55.446$  And so today we'll hear about

NOTE Confidence: 0.7699789

 $00:00:55.446 \longrightarrow 00:00:56.718$  this very exciting work.

 $00:00:56.720 \longrightarrow 00:00:59.218$  So Jorge, the floor is yours.

NOTE Confidence: 0.7699789

 $00:00:59.220 \longrightarrow 00:01:00.096$  Thanks Dan,

NOTE Confidence: 0.7699789

 $00:01:00.096 \longrightarrow 00:01:03.162$  thank you very much for the introduction.

NOTE Confidence: 0.7699789

 $00:01:03.170 \longrightarrow 00:01:05.258$  And yeah as then.

NOTE Confidence: 0.7699789

 $00:01:05.258 \longrightarrow 00:01:09.152$  Imply microbes and cancer are a lot

NOTE Confidence: 0.7699789

00:01:09.152 --> 00:01:13.076 more intertwined that many would think.

NOTE Confidence: 0.7699789

 $00:01:13.080 \longrightarrow 00:01:18.484$  If we start with the obvious that.

NOTE Confidence: 0.7699789

 $00:01:18.490 \longrightarrow 00:01:20.900 \ 20\%$  of cancers are caused

NOTE Confidence: 0.7699789

00:01:20.900 --> 00:01:22.346 by microbial infections.

NOTE Confidence: 0.7699789

 $00:01:22.350 \longrightarrow 00:01:25.558$  The you know of all these examples of

NOTE Confidence: 0.7699789

 $00{:}01{:}25.558 \rightarrow 00{:}01{:}28.609$  gastric cancer and helicobacter anogenital,

NOTE Confidence: 0.7699789

 $00:01:28.610 \longrightarrow 00:01:30.056$  cancer and HPV,

NOTE Confidence: 0.7699789

 $00:01:30.056 \longrightarrow 00:01:32.948$  and so on and so forth.

NOTE Confidence: 0.7699789

 $00:01:32.950 \longrightarrow 00:01:35.704$  So these are the known causes

NOTE Confidence: 0.7699789

 $00:01:35.704 \longrightarrow 00:01:38.250$  of microbial causes of cancer.

NOTE Confidence: 0.7699789

 $00:01:38.250 \longrightarrow 00:01:40.660$  That amount to that 20%.

00:01:40.660 --> 00:01:44.258 But by all accounts this is probably

NOTE Confidence: 0.7699789

 $00{:}01{:}44.258 \dashrightarrow 00{:}01{:}46.795$  rose underestimate in terms of

NOTE Confidence: 0.7699789

 $00:01:46.795 \longrightarrow 00:01:49.055$  the influence in the etiology

NOTE Confidence: 0.7699789

 $00:01:49.055 \longrightarrow 00:01:51.300$  of cancer of microbes.

NOTE Confidence: 0.7699789

00:01:51.300 --> 00:01:52.222 But Microsoft,

NOTE Confidence: 0.7699789

 $00:01:52.222 \longrightarrow 00:01:55.910$  either toying with cancer in many other ways.

NOTE Confidence: 0.7699789

 $00:01:55.910 \longrightarrow 00:01:56.764$  For example,

NOTE Confidence: 0.7699789

 $00:01:56.764 \longrightarrow 00:01:59.326$  the study of microbial pathogens really

NOTE Confidence: 0.7699789

 $00:01:59.326 \longrightarrow 00:02:01.249$  have provided fundamental knowledge

NOTE Confidence: 0.7699789

 $00:02:01.249 \longrightarrow 00:02:03.744$  for the understanding of cancer.

NOTE Confidence: 0.7699789

00:02:03.750 --> 00:02:05.004 You, of course,

NOTE Confidence: 0.7699789

 $00:02:05.004 \longrightarrow 00:02:07.512$  are aware that Uncle genes really

NOTE Confidence: 0.7699789

 $00:02:07.512 \longrightarrow 00:02:09.528$  were discovered through the

NOTE Confidence: 0.7699789

 $00{:}02{:}09.528 \dashrightarrow 00{:}02{:}12.048$  study of a chicken ritualize.

NOTE Confidence: 0.7699789

 $00:02:12.050 \longrightarrow 00:02:15.053$  And today the study of host pathogen

 $00:02:15.053 \longrightarrow 00:02:17.340$  interactions have provided insight into

NOTE Confidence: 0.7699789

 $00{:}02{:}17.340 \dashrightarrow 00{:}02{:}19.655$  cancer that are extremely important

NOTE Confidence: 0.7699789

 $00{:}02{:}19.655 \dashrightarrow 00{:}02{:}21.800$  for the fundamental knowledge.

NOTE Confidence: 0.7699789

 $00:02:21.800 \longrightarrow 00:02:23.832$  Of of these disease.

NOTE Confidence: 0.7699789

00:02:23.832 --> 00:02:24.848 Of course,

NOTE Confidence: 0.7699789

 $00:02:24.850 \longrightarrow 00:02:27.195$  infectious diseases as an entity

NOTE Confidence: 0.7699789

 $00{:}02{:}27.195 \dashrightarrow 00{:}02{:}29.540$  are really a significant challenge

NOTE Confidence: 0.7699789

 $00:02:29.610 \longrightarrow 00:02:31.986$  in the context of cancer patients.

NOTE Confidence: 0.7699789

 $00{:}02{:}31.990 \longrightarrow 00{:}02{:}34.524$  Many of the drugs that we administer

NOTE Confidence: 0.7699789

 $00:02:34.524 \longrightarrow 00:02:37.021$  to treat cancer or course have

NOTE Confidence: 0.7699789

 $00{:}02{:}37.021 \dashrightarrow 00{:}02{:}38.805$ immunosuppressive power an and

NOTE Confidence: 0.7699789

 $00:02:38.805 \longrightarrow 00:02:40.728$  that increases the susceptibility

NOTE Confidence: 0.7699789

 $00{:}02{:}40.728 \dashrightarrow 00{:}02{:}43.303$  of patients to infectious diseases

NOTE Confidence: 0.7699789

 $00{:}02{:}43.303 \dashrightarrow 00{:}02{:}46.500$  and imposes it challenge in many.

NOTE Confidence: 0.7699789

 $00:02:46.500 \longrightarrow 00:02:49.325$  In many therapeutic set settings.

NOTE Confidence: 0.7699789

 $00:02:49.330 \longrightarrow 00:02:52.849$  And of course, the the elephant in the room.

 $00:02:52.850 \longrightarrow 00:02:54.086$  The resident microbiome,

NOTE Confidence: 0.7699789

 $00{:}02{:}54.086 \dashrightarrow 00{:}02{:}57.929$  which in the last you know five years or so,

NOTE Confidence: 0.7699789

00:02:57.930 --> 00:03:00.667 is quickly emerging as a major factor,

NOTE Confidence: 0.7699789

00:03:00.670 --> 00:03:03.430 both in terms of cancer etiology

NOTE Confidence: 0.7699789

 $00:03:03.430 \longrightarrow 00:03:04.810$  and cancer treatment.

NOTE Confidence: 0.7699789

 $00:03:04.810 \longrightarrow 00:03:07.169$  So what what I'm trying to tell

NOTE Confidence: 0.7699789

 $00:03:07.169 \longrightarrow 00:03:09.481$  you here is something that it

NOTE Confidence: 0.7699789

 $00:03:09.481 \longrightarrow 00:03:12.330$  should be obvious and that this is

NOTE Confidence: 0.7699789

00:03:12.415 --> 00:03:15.000 an extremely important aspect of

NOTE Confidence: 0.7699789

00:03:15.000 --> 00:03:17.585 cancer biology and quite frankly,

NOTE Confidence: 0.7699789

 $00{:}03{:}17.590 \dashrightarrow 00{:}03{:}21.102$  is one of the most exciting times to

NOTE Confidence: 0.7699789

 $00:03:21.102 \longrightarrow 00:03:24.179$  be involved in this research space.

NOTE Confidence: 0.7699789

 $00{:}03{:}24.180 \dashrightarrow 00{:}03{:}26.352$  So the that's perhaps the reason

NOTE Confidence: 0.7699789

00:03:26.352 --> 00:03:29.644 why maybe some of us were a bit

NOTE Confidence: 0.7699789

 $00:03:29.644 \longrightarrow 00:03:31.412$  disappointed when the cancer

00:03:31.412 --> 00:03:33.707 microbiology piece of the Cancer

NOTE Confidence: 0.7699789

 $00{:}03{:}33.707 \dashrightarrow 00{:}03{:}35.045$  Center was interrupted.

NOTE Confidence: 0.7699789

 $00:03:35.050 \longrightarrow 00:03:35.886$  In fact,

NOTE Confidence: 0.7699789

 $00:03:35.886 \longrightarrow 00:03:39.230$  when I was invited to give this talk,

NOTE Confidence: 0.85875857

 $00:03:39.230 \longrightarrow 00:03:42.065$  I was invited as a member of

NOTE Confidence: 0.85875857

 $00:03:42.065 \longrightarrow 00:03:43.830$  the Cancer Microbiology Group,

NOTE Confidence: 0.85875857

 $00:03:43.830 \longrightarrow 00:03:45.610$  which now doesn't exist.

NOTE Confidence: 0.85875857

00:03:45.610 --> 00:03:47.835 And although I completely understand

NOTE Confidence: 0.85875857

 $00{:}03{:}47.835 \dashrightarrow 00{:}03{:}50.268$  why the leadership of the Cancer

NOTE Confidence: 0.85875857

 $00:03:50.268 \longrightarrow 00:03:52.183$  Center to please this step,

NOTE Confidence: 0.85875857

 $00{:}03{:}52.190 \dashrightarrow 00{:}03{:}55.480$  they had to tend to an impending.

NOTE Confidence: 0.85875857

 $00:03:55.480 \longrightarrow 00:03:59.788$  Cancer Center grant that.

NOTE Confidence: 0.85875857

00:03:59.790 --> 00:04:01.454 That obviously didn't take

NOTE Confidence: 0.85875857

 $00:04:01.454 \longrightarrow 00:04:03.118$  many of these things,

NOTE Confidence: 0.85875857

00:04:03.120 --> 00:04:06.448 and it is clear that you know cancer,

NOTE Confidence: 0.85875857

 $00:04:06.450 \longrightarrow 00:04:08.315$  microbiology or microbes really are

 $00:04:08.315 \longrightarrow 00:04:11.139$  not the this the so called cancer

NOTE Confidence: 0.85875857

 $00:04:11.139 \longrightarrow 00:04:13.344$  establishment from which reviewers will

NOTE Confidence: 0.85875857

 $00:04:13.344 \longrightarrow 00:04:16.848$  be drawn to review the Cancer Center grant.

NOTE Confidence: 0.85875857

 $00:04:16.850 \longrightarrow 00:04:19.340$  I'm not really friendly to the

NOTE Confidence: 0.85875857

 $00{:}04{:}19.340 \dashrightarrow 00{:}04{:}21.835$  concept of Micros, Ann and cancer.

NOTE Confidence: 0.85875857

 $00:04:21.835 \longrightarrow 00:04:23.495$  For for whatever reason,

NOTE Confidence: 0.85875857

 $00:04:23.500 \longrightarrow 00:04:25.164$  and even other considerations,

NOTE Confidence: 0.85875857

00:04:25.164 --> 00:04:27.660 other currencies that are used in

NOTE Confidence: 0.85875857

 $00{:}04{:}27.725 \dashrightarrow 00{:}04{:}29.740$  the evaluation of these grants,

NOTE Confidence: 0.85875857

 $00{:}04{:}29.740 \dashrightarrow 00{:}04{:}33.688$  such As for example in CI grants.

NOTE Confidence: 0.85875857

00:04:33.690 --> 00:04:34.410 You know,

NOTE Confidence: 0.85875857

 $00:04:34.410 \longrightarrow 00:04:36.930$  people work with my girls that that

NOTE Confidence: 0.85875857

 $00{:}04{:}36.930 \dashrightarrow 00{:}04{:}39.521$  don't score high on that because it

NOTE Confidence: 0.85875857

 $00:04:39.521 \longrightarrow 00:04:41.880$  will be a fundraising malpractice.

NOTE Confidence: 0.85875857

 $00:04:41.880 \longrightarrow 00:04:44.624$  If you can send your grant when

00:04:44.624 --> 00:04:47.339 I need to send it to NCI,

NOTE Confidence: 0.85875857

 $00:04:47.340 \longrightarrow 00:04:49.566$  which is much less generous and

NOTE Confidence: 0.85875857

 $00:04:49.566 \longrightarrow 00:04:52.020$  certainly less friendly to these courses.

NOTE Confidence: 0.85875857

00:04:52.020 --> 00:04:55.140 So I I although I totally understand these,

NOTE Confidence: 0.85875857

 $00:04:55.140 \longrightarrow 00:04:57.480$  I think is is an opportunity

NOTE Confidence: 0.85875857

 $00:04:57.480 \longrightarrow 00:04:58.650$  loss for leadership,

NOTE Confidence: 0.85875857

 $00:04:58.650 \longrightarrow 00:05:01.107$  particularly with the really the history

NOTE Confidence: 0.85875857

 $00:05:01.107 \longrightarrow 00:05:03.829$  of deal with the tremendous leadership.

NOTE Confidence: 0.85875857

 $00:05:03.830 \dashrightarrow 00:05:08.765$  People like Dundee Moniot or Charles Miller.

NOTE Confidence: 0.85875857

00:05:08.770 --> 00:05:10.846 In the space of Uncle Virus, for example,

NOTE Confidence: 0.85875857

 $00:05:10.846 \longrightarrow 00:05:13.849$  there is a lot of history here on this space.

NOTE Confidence: 0.85875857

 $00:05:13.850 \longrightarrow 00:05:15.880$  But life is life and the cancer

NOTE Confidence: 0.85875857

 $00:05:15.880 \longrightarrow 00:05:17.980$  establishment is the cancer establishment.

NOTE Confidence: 0.85875857

 $00:05:17.980 \longrightarrow 00:05:19.730$  This is the same establishment

NOTE Confidence: 0.85875857

 $00:05:19.730 \longrightarrow 00:05:22.450$  that 10 years ago or 20 years ago,

NOTE Confidence: 0.85875857

 $00:05:22.450 \longrightarrow 00:05:24.508$  worse naughty related to cancer immunology.

00:05:24.510 --> 00:05:27.606 It with people like blow it all the late,

NOTE Confidence: 0.85875857

 $00{:}05{:}27.610 \dashrightarrow 00{:}05{:}30.018$  allowing all that was advocating for it.

NOTE Confidence: 0.85875857

 $00:05:30.020 \longrightarrow 00:05:32.428$  And he was really honestly looked down.

NOTE Confidence: 0.85875857

 $00:05:32.430 \longrightarrow 00:05:34.150 \text{ I was a close collaborator}$ 

NOTE Confidence: 0.85875857

 $00:05:34.150 \longrightarrow 00:05:36.208$  the law and he always complained.

NOTE Confidence: 0.85875857

 $00:05:36.210 \longrightarrow 00:05:38.274$  Of course he was shielded by

NOTE Confidence: 0.85875857

 $00:05:38.274 \longrightarrow 00:05:39.650$  the Ludwig Cancer Center.

NOTE Confidence: 0.85875857

 $00:05:39.650 \longrightarrow 00:05:41.708$  He didn't have to worry about,

NOTE Confidence: 0.85875857

 $00:05:41.710 \longrightarrow 00:05:42.322$  but anyway,

NOTE Confidence: 0.85875857

 $00:05:42.322 \longrightarrow 00:05:45.720$  I think he said more of a loss opportunity.

NOTE Confidence: 0.85875857

00:05:45.720 --> 00:05:47.685 But I totally understand why

NOTE Confidence: 0.85875857

 $00:05:47.685 \longrightarrow 00:05:49.650$  this this decision was made,

NOTE Confidence: 0.85875857

 $00{:}05{:}49.650 \dashrightarrow 00{:}05{:}52.008$  so enough venting enough Priscilla Teising.

NOTE Confidence: 0.85875857

 $00:05:52.010 \longrightarrow 00:05:55.122$  Let's get back to business here and in

NOTE Confidence: 0.85875857

00:05:55.122 --> 00:05:58.299 order to put in context a little bit,

 $00:05:58.300 \longrightarrow 00:06:00.908$  what I will tell you briefly is is

NOTE Confidence: 0.85875857

 $00{:}06{:}00.908 \dashrightarrow 00{:}06{:}03.388$  to consider the general mechanisms by

NOTE Confidence: 0.85875857

 $00:06:03.388 \longrightarrow 00:06:06.022$  which microbes induce cancer and and

NOTE Confidence: 0.85875857

 $00:06:06.099 \longrightarrow 00:06:08.505$  there are two types of mechanisms.

NOTE Confidence: 0.85875857

 $00:06:08.510 \longrightarrow 00:06:09.599$  If you will.

NOTE Confidence: 0.85875857

 $00:06:09.599 \longrightarrow 00:06:12.140$  The direct Uncle Genesis and that is

NOTE Confidence: 0.85875857

 $00:06:12.218 \longrightarrow 00:06:15.123$  obvious when a virus is introduces an

NOTE Confidence: 0.85875857

 $00:06:15.123 \longrightarrow 00:06:18.282$  Uncle gene itself. This is of course.

NOTE Confidence: 0.85875857

 $00:06:18.282 \longrightarrow 00:06:21.540$  The mechanisms behind HPB or a BB,

NOTE Confidence: 0.85875857

 $00:06:21.540 \longrightarrow 00:06:22.582$  for example.

NOTE Confidence: 0.85875857

 $00{:}06{:}22.582 \dashrightarrow 00{:}06{:}25.708$  Or when it when they integration

NOTE Confidence: 0.85875857

00:06:25.708 --> 00:06:28.459 event itself access and origin,

NOTE Confidence: 0.85875857

 $00:06:28.460 \longrightarrow 00:06:30.865$  because obviously the viruses integrate

NOTE Confidence: 0.85875857

 $00{:}06{:}30.865 \to 00{:}06{:}34.247$  upstream of some gene that can drive

NOTE Confidence: 0.85875857

 $00:06:34.247 \longrightarrow 00:06:36.487$  sort of proliferation and growth.

NOTE Confidence: 0.85875857

 $00:06:36.490 \longrightarrow 00:06:39.316$  That's that's direct on Go Genesis,

 $00:06:39.320 \longrightarrow 00:06:41.680$  but arguably more common is

NOTE Confidence: 0.85875857

 $00{:}06{:}41.680 \dashrightarrow 00{:}06{:}43.568$  the indirect organ Genesis,

NOTE Confidence: 0.85875857

 $00:06:43.570 \longrightarrow 00:06:45.930$  and this takes several forms.

NOTE Confidence: 0.85875857

 $00:06:45.930 \longrightarrow 00:06:48.762$  For example the form in which

NOTE Confidence: 0.85875857

 $00:06:48.762 \longrightarrow 00:06:50.650$  viruses in a cost,

NOTE Confidence: 0.85875857

 $00{:}06{:}50.650 \dashrightarrow 00{:}06{:}52.174$ immunosuppression and immunosuppression

NOTE Confidence: 0.85875857

 $00:06:52.174 \longrightarrow 00:06:53.698$  activates for example.

NOTE Confidence: 0.85875857

 $00:06:53.700 \longrightarrow 00:06:55.288$  Other two more viruses.

NOTE Confidence: 0.85875857

 $00{:}06{:}55.288 \dashrightarrow 00{:}06{:}57.670$  In the case of Kaposi sarcoma,

NOTE Confidence: 0.85875857

00:06:57.670 --> 00:06:59.660 is an HIV HIV infection.

NOTE Confidence: 0.85875857

 $00:06:59.660 \longrightarrow 00:07:02.432$  It comes to mind or when viruses

NOTE Confidence: 0.85875857

 $00:07:02.432 \longrightarrow 00:07:04.024$  viral infection, for example,

NOTE Confidence: 0.85875857

 $00{:}07{:}04.024 \dashrightarrow 00{:}07{:}05.612$  triggers chromosome instability or

NOTE Confidence: 0.85875857

 $00{:}07{:}05.612 \dashrightarrow 00{:}07{:}07.200$  translocation that eventually die.

NOTE Confidence: 0.79306287

 $00:07:07.200 \longrightarrow 00:07:09.748$  Of course, leads to cancer and other

00:07:09.748 --> 00:07:11.769 aspects of the Director Genesis

NOTE Confidence: 0.79306287

00:07:11.769 --> 00:07:14.337 more related to what I'm being,

NOTE Confidence: 0.79306287

 $00:07:14.340 \longrightarrow 00:07:17.516$  I'm going to be telling you today is,

NOTE Confidence: 0.79306287

00:07:17.520 --> 00:07:19.448 for example, chronic inflammation,

NOTE Confidence: 0.79306287

 $00:07:19.448 \longrightarrow 00:07:22.340$  which is very well established to

NOTE Confidence: 0.79306287

 $00:07:22.413 \longrightarrow 00:07:24.537$  be linked to Uncle Genesis.

NOTE Confidence: 0.79306287

 $00:07:24.540 \longrightarrow 00:07:26.184$  The production of proinflammatory

NOTE Confidence: 0.79306287

00:07:26.184 --> 00:07:28.239 cytokines that have growth promoting

NOTE Confidence: 0.79306287

 $00{:}07{:}28.239 \dashrightarrow 00{:}07{:}30.247$  abilities combined with oxygen radicals.

NOTE Confidence: 0.79306287

 $00:07:30.250 \longrightarrow 00:07:33.169$  They have a mutation or mutagenesis ability

NOTE Confidence: 0.79306287

 $00{:}07{:}33.169 \dashrightarrow 00{:}07{:}35.958$  leads to setting the stage for Franco,

NOTE Confidence: 0.79306287

 $00:07:35.960 \longrightarrow 00:07:37.512$  Genesis is the case,

NOTE Confidence: 0.79306287

 $00{:}07{:}37.512 \dashrightarrow 00{:}07{:}39.064$  for example with Helicobacter

NOTE Confidence: 0.79306287

00:07:39.064 --> 00:07:40.859 pylori and gastric cancer,

NOTE Confidence: 0.79306287

 $00:07:40.860 \longrightarrow 00:07:43.856$  and in addition something that has been

NOTE Confidence: 0.79306287

 $00:07:43.856 \longrightarrow 00:07:46.563$  emerging over the last few years and

 $00:07:46.563 \longrightarrow 00:07:49.556$  that we sort of Pioneer in this area

NOTE Confidence: 0.79306287

 $00{:}07{:}49.556 \dashrightarrow 00{:}07{:}52.214$  is the fact that certain organisms

NOTE Confidence: 0.79306287

00:07:52.214 --> 00:07:54.651 really produce direct Gina toxins

NOTE Confidence: 0.79306287

 $00:07:54.651 \longrightarrow 00:07:57.753$  that will drive the oncogenic event.

NOTE Confidence: 0.79306287

 $00{:}07{:}57.760 \dashrightarrow 00{:}08{:}00.576$  So I say alluded these last two are

NOTE Confidence: 0.79306287

 $00:08:00.576 \longrightarrow 00:08:03.440$  the ones more relevant to bacteria,

NOTE Confidence: 0.79306287

 $00:08:03.440 \longrightarrow 00:08:05.888$  which is the type of microbes

NOTE Confidence: 0.79306287

 $00:08:05.888 \longrightarrow 00:08:08.320$  that we study in the lab.

NOTE Confidence: 0.79306287

 $00:08:08.320 \longrightarrow 00:08:10.552$  So bacterial is in this context

NOTE Confidence: 0.79306287

 $00{:}08{:}10.552 \dashrightarrow 00{:}08{:}12.040$  bacterial colonization leads to

NOTE Confidence: 0.79306287

00:08:12.105 --> 00:08:13.761 both inflammation and genotoxin

NOTE Confidence: 0.79306287

 $00:08:13.761 \longrightarrow 00:08:16.245$  production and exposures of tissues to

NOTE Confidence: 0.79306287

 $00{:}08{:}16.305 \dashrightarrow 00{:}08{:}17.985$  genotoxin and therefore predisposing

NOTE Confidence: 0.79306287

 $00:08:17.985 \longrightarrow 00:08:20.085$  those tissues to to cancel.

NOTE Confidence: 0.79306287

 $00:08:20.090 \longrightarrow 00:08:23.121$  What I'm gonna be telling you today

00:08:23.121 --> 00:08:26.088 is the paradigm of two organisms that

NOTE Confidence: 0.79306287

 $00:08:26.088 \longrightarrow 00:08:29.354$  we study in the lab. Both of them.

NOTE Confidence: 0.79306287

 $00{:}08{:}29.354 \dashrightarrow 00{:}08{:}31.066$  These organisms are salmonella

NOTE Confidence: 0.79306287

 $00:08:31.066 \longrightarrow 00:08:32.350$  and campylobacter jejuni.

NOTE Confidence: 0.79306287

 $00:08:32.350 \longrightarrow 00:08:34.912$  Both of them have been very

NOTE Confidence: 0.79306287

 $00:08:34.912 \longrightarrow 00:08:35.766$  strongly epidemiological.

NOTE Confidence: 0.79306287

 $00:08:35.770 \longrightarrow 00:08:37.940$  He associated with the development

NOTE Confidence: 0.79306287

 $00{:}08{:}37.940 \dashrightarrow 00{:}08{:}39.676$  of cancer Campylobacter jejuni

NOTE Confidence: 0.79306287

00:08:39.676 --> 00:08:41.770 associated with an intestinal lymphoma,

NOTE Confidence: 0.79306287

00:08:41.770 --> 00:08:43.430 and while Salmonella Typhi,

NOTE Confidence: 0.79306287

 $00:08:43.430 \longrightarrow 00:08:46.648$  one of these family that we study in

NOTE Confidence: 0.79306287

00:08:46.648 --> 00:08:49.240 the lab is really a major cause of

NOTE Confidence: 0.79306287

 $00{:}08{:}49.323 \dashrightarrow 00{:}08{:}51.435$  Gallbladder cancer and Gallbladder

NOTE Confidence: 0.79306287

 $00:08:51.435 \longrightarrow 00:08:55.085$  cancer in endemic areas is actually one

NOTE Confidence: 0.79306287

 $00:08:55.085 \longrightarrow 00:08:58.410$  of the main cancers that affect those.

NOTE Confidence: 0.79306287

 $00:08:58.410 \longrightarrow 00:09:01.620$  Individuals and it infections with

00:09:01.620 --> 00:09:04.188 Salmonella Typhi and associated

NOTE Confidence: 0.79306287

 $00{:}09{:}04.188 \to 00{:}09{:}06.560$  with a 204 risk of hip,

NOTE Confidence: 0.79306287 00:09:06.560 --> 00:09:07.101 hip, NOTE Confidence: 0.79306287

00:09:07.101 --> 00:09:08.724 hepatobiliary carcinoma and

NOTE Confidence: 0.79306287

00:09:08.724 --> 00:09:09.806 Gallbladder cancer,

NOTE Confidence: 0.79306287

 $00:09:09.810 \longrightarrow 00:09:14.038$  so these are important causes of cancer

NOTE Confidence: 0.79306287

 $00:09:14.038 \longrightarrow 00:09:17.052$  which incidentally are not in that

NOTE Confidence: 0.79306287

00:09:17.052 --> 00:09:21.860 20% statistic that I told you about.

NOTE Confidence: 0.79306287

 $00:09:21.860 --> 00:09:22.246 \ \mathrm{Now},$ 

NOTE Confidence: 0.79306287

 $00:09:22.246 \longrightarrow 00:09:24.176$  in the case of Campylobacter,

NOTE Confidence: 0.79306287

 $00:09:24.180 \longrightarrow 00:09:26.508$  what we discovered that was sort

NOTE Confidence: 0.79306287

 $00{:}09{:}26.508 \dashrightarrow 00{:}09{:}28.853$  of central to understand how these

NOTE Confidence: 0.79306287

 $00{:}09{:}28.853 \dashrightarrow 00{:}09{:}31.019$  organisms linked to oncogenesis is a

NOTE Confidence: 0.79306287

00:09:31.019 --> 00:09:33.389 is the characterization of a toxin

NOTE Confidence: 0.79306287

 $00:09:33.389 \longrightarrow 00:09:36.321$  that we did almost two decades ago

00:09:36.321 --> 00:09:40.248 actually scary more than two decades ago?

NOTE Confidence: 0.79306287

 $00{:}09{:}40.250 \dashrightarrow 00{:}09{:}42.966$  That he said to xin that caught our

NOTE Confidence: 0.79306287

 $00:09:42.966 \longrightarrow 00:09:45.897$  attention because of what you see here in in.

NOTE Confidence: 0.79306287

 $00:09:45.900 \longrightarrow 00:09:46.959$  In these images,

NOTE Confidence: 0.79306287

 $00:09:46.959 \longrightarrow 00:09:49.077$  these are cells that are intoxicated.

NOTE Confidence: 0.79306287

 $00:09:49.080 \longrightarrow 00:09:51.824$  You see them very much expanded with a

NOTE Confidence: 0.79306287

 $00:09:51.824 \longrightarrow 00:09:53.955$  large nuclei in comparison to control

NOTE Confidence: 0.79306287

 $00:09:53.955 \longrightarrow 00:09:56.490$  cell at the same excuse me Jorge,

NOTE Confidence: 0.79306287

 $00{:}09{:}56.490 --> 00{:}09{:}57.549$ your your slide

NOTE Confidence: 0.8167658

 $00:09:57.550 \longrightarrow 00:09:59.668$  is not. It did not advance.

NOTE Confidence: 0.820451730769231

 $00:10:00.120 \longrightarrow 00:10:01.347$  Papa you mean?

NOTE Confidence: 0.820451730769231

 $00{:}10{:}01.347 \dashrightarrow 00{:}10{:}05.640$  I mean what they have you on the 1st slide?

NOTE Confidence: 0.820451730769231

 $00:10:05.640 \longrightarrow 00:10:09.060$  Oh gosh, that's that's not good.

NOTE Confidence: 0.820451730769231

00:10:09.060 --> 00:10:11.780 That can you see them this way now?

NOTE Confidence: 0.820451730769231

 $00:10:11.780 \longrightarrow 00:10:14.484$  Yeah, that I can see those OK when

NOTE Confidence: 0.820451730769231

 $00:10:14.484 \longrightarrow 00:10:17.558$  I when I do it that way because OK,

 $00:10:17.560 \longrightarrow 00:10:18.580$  yeah unfortunately because

NOTE Confidence: 0.820451730769231

 $00{:}10{:}18.580 \dashrightarrow 00{:}10{:}20.620$  whatever it would have been easier.

NOTE Confidence: 0.820451730769231

 $00:10:20.620 \longrightarrow 00:10:23.000$  But thank you for letting me know.

NOTE Confidence: 0.820451730769231

 $00:10:23.000 \longrightarrow 00:10:25.720$  OK so anyway, so here it is the.

NOTE Confidence: 0.76506776

00:10:28.960 --> 00:10:31.402 OK, so this image is showing

NOTE Confidence: 0.76506776

 $00:10:31.402 \longrightarrow 00:10:34.754$  you the the cells that have been

NOTE Confidence: 0.76506776

 $00:10:34.754 \longrightarrow 00:10:36.930$  intoxicated with this toxin,

NOTE Confidence: 0.76506776

 $00:10:36.930 \longrightarrow 00:10:39.194$  showing this unusual morphology.

NOTE Confidence: 0.76506776

 $00{:}10{:}39.194 \dashrightarrow 00{:}10{:}42.024$  In comparison we control cell

NOTE Confidence: 0.76506776

 $00{:}10{:}42.024 \dashrightarrow 00{:}10{:}45.352$  and the reason these cells have

NOTE Confidence: 0.76506776

 $00{:}10{:}45.352 \dashrightarrow 00{:}10{:}47.488$  that morphology is becaused.

NOTE Confidence: 0.76506776

 $00{:}10{:}47.490 \dashrightarrow 00{:}10{:}50.698$  The cells are stuck on the G2M phase

NOTE Confidence: 0.76506776

 $00{:}10{:}50.698 {\:{\mbox{--}}\!>}\ 00{:}10{:}53.828$  of the cell cycle and we found

NOTE Confidence: 0.76506776

 $00:10:53.828 \longrightarrow 00:10:57.141$  that the reason for that is that

NOTE Confidence: 0.76506776

 $00:10:57.141 \longrightarrow 00:11:00.075$  this toxin that we had discovered.

00:11:00.080 --> 00:11:03.360 It has a genotoxicity DNA damage in capacity,

NOTE Confidence: 0.76506776

 $00:11:03.360 \longrightarrow 00:11:05.844$  those this is a toxin typical

NOTE Confidence: 0.76506776

 $00:11:05.844 \longrightarrow 00:11:07.870$  toxin of we call AB.

NOTE Confidence: 0.76506776

 $00:11:07.870 \longrightarrow 00:11:10.740$  Toxins have two two types of parts.

NOTE Confidence: 0.76506776

00:11:10.740 --> 00:11:13.200 If you will the be part,

NOTE Confidence: 0.76506776

 $00:11:13.200 \longrightarrow 00:11:16.456$  which is what targets the payload to a

NOTE Confidence: 0.76506776

 $00{:}11{:}16.456 \dashrightarrow 00{:}11{:}18.938$  particular cell and the payload part.

NOTE Confidence: 0.76506776

 $00{:}11{:}18.940 \dashrightarrow 00{:}11{:}21.971$  The nucleus is is an endonuclease is

NOTE Confidence: 0.76506776

00:11:21.971 --> 00:11:24.531 actually an unusual in the nucleus

NOTE Confidence: 0.76506776

00:11:24.531 --> 00:11:26.895 in the sense that primary amino

NOTE Confidence: 0.76506776

 $00{:}11{:}26.895 \mathrel{--}{>} 00{:}11{:}28.916$  acid sequence would not overtly

NOTE Confidence: 0.76506776

 $00:11:28.916 \longrightarrow 00:11:32.340$  tell you that this is a new case.

NOTE Confidence: 0.76506776

 $00:11:32.340 \longrightarrow 00:11:36.740$  But when you look at the atomic structure,

NOTE Confidence: 0.76506776

 $00{:}11{:}36.740 \dashrightarrow 00{:}11{:}40.765$  you can make out the catalytic side.

NOTE Confidence: 0.76506776

 $00:11:40.770 \longrightarrow 00:11:44.874$  So so this is a typical case of

NOTE Confidence: 0.76506776

 $00:11:44.874 \longrightarrow 00:11:48.518$  genotoxin that is responsible for for

00:11:48.518 --> 00:11:52.268 driving driving the day on today.

NOTE Confidence: 0.8201903

00:11:54.500 --> 00:11:57.930 Cancer development and in fact just recently,

NOTE Confidence: 0.8201903

 $00:11:57.930 \longrightarrow 00:12:00.460$  this has been formally demonstrated

NOTE Confidence: 0.8201903

 $00:12:00.460 \longrightarrow 00:12:04.243$  in an animal model that that this

NOTE Confidence: 0.8201903

 $00:12:04.243 \longrightarrow 00:12:07.158$  toxin is responsible for Campylobacter

NOTE Confidence: 0.8201903

 $00{:}12{:}07.158 \dashrightarrow 00{:}12{:}10.538$  jejuni's ability to promote cancer so.

NOTE Confidence: 0.8201903

00:12:10.540 --> 00:12:13.308 It's kind of awkward to have to advise

NOTE Confidence: 0.8201903

 $00:12:13.308 \longrightarrow 00:12:16.240$  it like this, but I will go ahead.

NOTE Confidence: 0.8201903

 $00:12:16.240 \longrightarrow 00:12:18.388$  So the second example is Salmonella

NOTE Confidence: 0.8201903

 $00{:}12{:}18.388 \rightarrow 00{:}12{:}21.296$  Typhi and I need to tell you that

NOTE Confidence: 0.8201903

 $00:12:21.296 \longrightarrow 00:12:23.819$  the the basic about something that I

NOTE Confidence: 0.8201903

 $00:12:23.819 \longrightarrow 00:12:25.883$  think people things in context again

NOTE Confidence: 0.8201903

00:12:25.883 --> 00:12:28.340 and that is that someone had typhus

NOTE Confidence: 0.8201903

 $00:12:28.340 \longrightarrow 00:12:30.115$  and exclusive pathogen of humans.

NOTE Confidence: 0.8201903

 $00:12:30.120 \longrightarrow 00:12:31.584$  It causes typhoid fever.

00:12:31.584 --> 00:12:34.389 One of those historical diseases if you will,

NOTE Confidence: 0.8201903

 $00{:}12{:}34.390 \dashrightarrow 00{:}12{:}36.679$  but important for Genesis is the fact

NOTE Confidence: 0.8201903

 $00:12:36.679 \longrightarrow 00:12:39.020$  that those that survived the disease,

NOTE Confidence: 0.8201903

 $00:12:39.020 \longrightarrow 00:12:41.638$  many of them go on to persistently

NOTE Confidence: 0.8201903

00:12:41.638 --> 00:12:42.760 harbored the Organism.

NOTE Confidence: 0.8201903

 $00:12:42.760 \longrightarrow 00:12:45.749$  Within the Gallbladder and that is where

NOTE Confidence: 0.8201903

 $00:12:45.749 \longrightarrow 00:12:48.693$  the rubber meets the road and that

NOTE Confidence: 0.8201903

 $00:12:48.693 \longrightarrow 00:12:51.075$  is the reason why those individuals

NOTE Confidence: 0.8201903

 $00{:}12{:}51.150 \dashrightarrow 00{:}12{:}53.135$  that are harboring salmonella typing

NOTE Confidence: 0.8201903

 $00:12:53.135 \longrightarrow 00:12:56.356$  in the in the in the areas are

NOTE Confidence: 0.8201903

 $00{:}12{:}56.356 \dashrightarrow 00{:}12{:}58.416$  prone to develop Gallbladder cancer.

NOTE Confidence: 0.8201903

 $00:12:58.420 \longrightarrow 00:13:00.891$  And in the case of Salmonella the

NOTE Confidence: 0.8201903

 $00:13:00.891 \longrightarrow 00:13:02.990$  paradigm is slightly different than

NOTE Confidence: 0.8201903

 $00:13:02.990 \longrightarrow 00:13:05.420$  the paradigm in Campylobacter jejuni.

NOTE Confidence: 0.8201903

00:13:05.420 --> 00:13:07.480 But it shares it remarkably,

NOTE Confidence: 0.8201903

 $00:13:07.480 \longrightarrow 00:13:10.357$  is shares more than what would expect.

 $00:13:10.360 \longrightarrow 00:13:13.640$  You need to think in terms of evolution

NOTE Confidence: 0.8201903

 $00{:}13{:}13.640 \dashrightarrow 00{:}13{:}16.240$  that Campylobacter and Salmonella are they.

NOTE Confidence: 0.8201903

 $00:13:16.240 \longrightarrow 00:13:18.320$  Couldn't be more far apart.

NOTE Confidence: 0.8201903

00:13:18.320 --> 00:13:20.390 One is an epsilon bacteria,

NOTE Confidence: 0.8201903

 $00{:}13{:}20.390 \dashrightarrow 00{:}13{:}22.470$  the other is a gamma proteobacteria.

NOTE Confidence: 0.8201903

00:13:22.470 --> 00:13:24.795 It's like absolutely no evolutionary

NOTE Confidence: 0.8201903

 $00:13:24.795 \longrightarrow 00:13:28.058$  connection and yet what is remarkable is

NOTE Confidence: 0.8201903

 $00:13:28.058 \longrightarrow 00:13:31.054$  that we discover a toxin in Salmonella

NOTE Confidence: 0.8201903

 $00{:}13{:}31.054 \dashrightarrow 00{:}13{:}33.559$  typhi that we call typhoid toxin.

NOTE Confidence: 0.8201903

 $00:13:33.560 \longrightarrow 00:13:35.882$  That also has the ability to

NOTE Confidence: 0.8201903

00:13:35.882 --> 00:13:37.043 induce DNA damage,

NOTE Confidence: 0.8201903

 $00:13:37.050 \longrightarrow 00:13:39.378$  as shown here in this image,

NOTE Confidence: 0.8201903

 $00{:}13{:}39.380 \dashrightarrow 00{:}13{:}41.708$  and when we characterize this toxin,

NOTE Confidence: 0.8201903

 $00:13:41.710 \longrightarrow 00:13:43.756$  we were surprised to see that

NOTE Confidence: 0.8201903

 $00:13:43.756 \longrightarrow 00:13:46.125$  the active subunit of this toxin

00:13:46.125 --> 00:13:47.529 was virtually identical,

NOTE Confidence: 0.8201903

 $00:13:47.530 \longrightarrow 00:13:49.972$  that the active subunit of the

NOTE Confidence: 0.8201903

 $00:13:49.972 \longrightarrow 00:13:51.600$  completely unrelated toxin Curry

NOTE Confidence: 0.8201903

00:13:51.669 --> 00:13:53.349 by camping of active June.

NOTE Confidence: 0.8201903

 $00:13:53.350 \longrightarrow 00:13:55.672$  So this is really a remarkable

NOTE Confidence: 0.8201903

 $00:13:55.672 \longrightarrow 00:13:56.833$  piece of evolution.

NOTE Confidence: 0.8201903

 $00:13:56.840 \longrightarrow 00:13:59.423$  This is one of those head turning

NOTE Confidence: 0.8201903

00:13:59.423 --> 00:14:01.810 toxins that actually evolution put it

NOTE Confidence: 0.8201903

 $00{:}14{:}01.810 \dashrightarrow 00{:}14{:}04.210$  together by fusing two toxins, one.

NOTE Confidence: 0.8201903

00:14:04.210 --> 00:14:06.940 That some of you may be familiar,

NOTE Confidence: 0.8201903

00:14:06.940 --> 00:14:08.136 it called pertussis toxin,

NOTE Confidence: 0.8201903

 $00:14:08.136 \longrightarrow 00:14:11.087$  is what makes you a what is central for

NOTE Confidence: 0.8201903

 $00:14:11.087 \longrightarrow 00:14:12.917$  the pathogenesis of whooping cough.

NOTE Confidence: 0.8201903

 $00:14:12.920 \longrightarrow 00:14:15.244$  And then these other talks in that

NOTE Confidence: 0.8201903

 $00:14:15.244 \longrightarrow 00:14:16.240$  I described earlier.

NOTE Confidence: 0.8201903

 $00:14:16.240 \longrightarrow 00:14:18.226$  They cite a little distending toxin,

 $00{:}14{:}18.230 \dashrightarrow 00{:}14{:}20.253$  so this lower part of the talks

NOTE Confidence: 0.8201903

 $00{:}14{:}20.253 \mathrel{--}{>} 00{:}14{:}22.220$  in comes from pertussis toxin,

NOTE Confidence: 0.8201903

 $00:14:22.220 \longrightarrow 00:14:24.170$  and this upper Paradox income from

NOTE Confidence: 0.8201903

00:14:24.170 --> 00:14:25.870 side a little extended talks,

NOTE Confidence: 0.8201903

00:14:25.870 --> 00:14:27.380 so evolution hook them together

NOTE Confidence: 0.8201903

 $00:14:27.380 \longrightarrow 00:14:29.324$  to make this head turning toxin

NOTE Confidence: 0.8201903

00:14:29.324 --> 00:14:30.848 that Salmonella typhi encodes,

NOTE Confidence: 0.8201903

 $00{:}14{:}30.850 \dashrightarrow 00{:}14{:}33.272$  and that it is responsible for the

NOTE Confidence: 0.8201903

00:14:33.272 --> 00:14:35.000 genotoxicity of these organisms.

NOTE Confidence: 0.8201903

00:14:35.000 --> 00:14:37.064 And easy sent unusual toxin in

NOTE Confidence: 0.8201903

00:14:37.064 --> 00:14:39.023 many different ways that I don't

NOTE Confidence: 0.8201903

 $00:14:39.023 \longrightarrow 00:14:40.318$  have time to go into,

NOTE Confidence: 0.8201903

 $00{:}14{:}40.320 \dashrightarrow 00{:}14{:}42.574$  but one of the remarkable ways in

NOTE Confidence: 0.8201903

 $00:14:42.574 \longrightarrow 00:14:45.019$  which this toxin is unique is that it

NOTE Confidence: 0.8201903

 $00:14:45.019 \longrightarrow 00:14:47.210$  is other patient to the human host.

 $00:14:47.210 \longrightarrow 00:14:49.394$  And what do I mean by that?

NOTE Confidence: 0.8201903

00:14:49.400 --> 00:14:51.278 Well, the receptor for these talks,

NOTE Confidence: 0.8201903

 $00:14:51.280 \longrightarrow 00:14:52.440$  you know the receptors.

NOTE Confidence: 0.8201903

 $00:14:52.440 \longrightarrow 00:14:54.720$  I should say we discovered two proteins,

NOTE Confidence: 0.8201903

00:14:54.720 --> 00:14:55.896 part of policing,

NOTE Confidence: 0.8201903

 $00:14:55.896 \longrightarrow 00:14:58.950$  one in epithelial cells and CD 45 in.

NOTE Confidence: 0.8201903

00:14:58.950 --> 00:15:00.042 In immune cells,

NOTE Confidence: 0.8201903

 $00:15:00.042 \longrightarrow 00:15:02.226$  but what is important here is

NOTE Confidence: 0.8201903

 $00:15:02.226 \longrightarrow 00:15:04.727$  what does the toxin see on this

NOTE Confidence: 0.8201903

 $00:15:04.727 \longrightarrow 00:15:06.099$  block of proteins and

NOTE Confidence: 0.76375777

 $00{:}15{:}06.174 \dashrightarrow 00{:}15{:}09.030$  is the glycan power and we through like

NOTE Confidence: 0.76375777

 $00:15:09.030 \longrightarrow 00:15:11.385$  Andres and other types of studies for

NOTE Confidence: 0.76375777

 $00:15:11.385 \longrightarrow 00:15:13.466$  to address these kinds of questions

NOTE Confidence: 0.76375777

 $00{:}15{:}13.466 \dashrightarrow 00{:}15{:}15.764$  we discovered that what What Typhoid

NOTE Confidence: 0.76375777

 $00:15:15.764 \longrightarrow 00:15:18.407$  toxin likes if you will is glycans

NOTE Confidence: 0.76375777

 $00{:}15{:}18.407 \dashrightarrow 00{:}15{:}20.187$  terminated in the sitting room.

 $00:15:20.190 \longrightarrow 00:15:22.374$  We know that many Kacian hooked to

NOTE Confidence: 0.76375777

 $00{:}15{:}22.374 \dashrightarrow 00{:}15{:}24.994$  galactose and and to glucose or setting

NOTE Confidence: 0.76375777

 $00:15:24.994 \longrightarrow 00:15:27.024$  glucosamine in this particular fashion.

NOTE Confidence: 0.76375777

 $00:15:27.030 \longrightarrow 00:15:28.960$  And why is this relevant?

NOTE Confidence: 0.76375777

 $00{:}15{:}28.960 \dashrightarrow 00{:}15{:}31.414$  Well, this is important because you

NOTE Confidence: 0.76375777

 $00:15:31.414 \longrightarrow 00:15:34.342$  may not know these or many of you

NOTE Confidence: 0.76375777

 $00:15:34.342 \longrightarrow 00:15:36.725$  May is that we humans are actually

NOTE Confidence: 0.76375777

00:15:36.725 --> 00:15:39.647 rather unusual mammals in many ways,

NOTE Confidence: 0.76375777

 $00:15:39.650 \longrightarrow 00:15:42.378$  and one of the ways in which terribly

NOTE Confidence: 0.76375777

 $00:15:42.378 \longrightarrow 00:15:45.197$  unusual is in our glycosylation pattern.

NOTE Confidence: 0.76375777

 $00{:}15{:}45.200 \dashrightarrow 00{:}15{:}47.170$  All our sciullo glycans are

NOTE Confidence: 0.76375777

 $00:15:47.170 \longrightarrow 00:15:49.550$  terminated in a city neuraminic acid,

NOTE Confidence: 0.76375777

 $00{:}15{:}49.550 \dashrightarrow 00{:}15{:}51.926$  but all other mammals in fact,

NOTE Confidence: 0.76375777

00:15:51.930 --> 00:15:53.910 like answer, terminated in Blakely,

NOTE Confidence: 0.76375777

00:15:53.910 --> 00:15:54.730 neuraminic acid,

 $00:15:54.730 \longrightarrow 00:15:57.190$  and the reason is that the

NOTE Confidence: 0.76375777

 $00:15:57.190 \longrightarrow 00:15:59.510$  enzyme that is responsible for.

NOTE Confidence: 0.76375777

 $00:15:59.510 \longrightarrow 00:16:02.000$  Can you see this slide and?

NOTE Confidence: 0.76375777

 $00:16:02.000 \longrightarrow 00:16:02.371$  Maybe.

NOTE Confidence: 0.76375777

 $00:16:02.371 \longrightarrow 00:16:04.597$  Well, whatever I continuously the inside

NOTE Confidence: 0.76375777

 $00{:}16{:}04.597 \dashrightarrow 00{:}16{:}07.038$  that is responsible for putting these acts.

NOTE Confidence: 0.76375777

 $00:16:07.040 \longrightarrow 00:16:09.200$  Oxygen here is mutated in humans.

NOTE Confidence: 0.76375777

 $00:16:09.200 \longrightarrow 00:16:11.482$  We have a pseudogene there and therefore

NOTE Confidence: 0.76375777

 $00{:}16{:}11.482 \dashrightarrow 00{:}16{:}14.692$  we are unique in that fashion and typhoid

NOTE Confidence: 0.76375777

00:16:14.692 --> 00:16:16.428 toxin combined likens exclusively

NOTE Confidence: 0.76375777

 $00{:}16{:}16.428 {\:\dashrightarrow\:} 00{:}16{:}18.197$  terminated in a city in America.

NOTE Confidence: 0.76375777

00:16:18.200 --> 00:16:19.187 And in fact,

NOTE Confidence: 0.76375777

00:16:19.187 --> 00:16:21.490 if you just change one oxidant in

NOTE Confidence: 0.76375777

00:16:21.562 --> 00:16:23.836 any of these glycans that Typhoid

NOTE Confidence: 0.76375777

 $00:16:23.836 \longrightarrow 00:16:26.138$  toxin likes and you already meaning

NOTE Confidence: 0.76375777

00:16:26.138 --> 00:16:28.994 in in an array make like an array,

 $00:16:29.000 \longrightarrow 00:16:30.800$  typhoid toxin does not bind.

NOTE Confidence: 0.76375777

 $00{:}16{:}30.800 \dashrightarrow 00{:}16{:}33.390$  It also has the ability to distinguish.

NOTE Confidence: 0.76375777

 $00:16:33.390 \longrightarrow 00:16:35.580$  Just one Atom of oxygen.

NOTE Confidence: 0.76375777

 $00:16:35.580 \longrightarrow 00:16:37.685$  Remarkable piece of evolution that

NOTE Confidence: 0.76375777

 $00:16:37.685 \longrightarrow 00:16:40.764$  makes it able to target human cells

NOTE Confidence: 0.76375777

 $00:16:40.764 \longrightarrow 00:16:42.994$  and have that oncogenic effect.

NOTE Confidence: 0.76375777

 $00:16:43.000 \longrightarrow 00:16:45.622$  But in addition to having a

NOTE Confidence: 0.76375777

 $00:16:45.622 \longrightarrow 00:16:46.496$  genotoxin somewhere,

NOTE Confidence: 0.76375777

 $00:16:46.500 \longrightarrow 00:16:49.116$  typhi is actually has the 241.

NOTE Confidence: 0.76375777

 $00:16:49.120 \longrightarrow 00:16:50.599$  In other words,

NOTE Confidence: 0.76375777

 $00:16:50.599 \longrightarrow 00:16:53.064$  is also the chronic inflammation

NOTE Confidence: 0.76375777

 $00:16:53.064 \longrightarrow 00:16:56.433$  part that plays a role in the

NOTE Confidence: 0.76375777

 $00{:}16{:}56.433 \dashrightarrow 00{:}16{:}58.728$  Uncle Genesis of Salmonella Typhi.

NOTE Confidence: 0.76375777

 $00:16:58.730 \longrightarrow 00:17:01.747$  And so it's something that I think

NOTE Confidence: 0.76375777

00:17:01.747 --> 00:17:04.092 causes chronic inflammation of the

00:17:04.092 --> 00:17:06.527 Gallbladder and that chronic inflammation,

NOTE Confidence: 0.76375777

 $00:17:06.530 \longrightarrow 00:17:08.334$  as is well known,

NOTE Confidence: 0.76375777

 $00{:}17{:}08.334 \dashrightarrow 00{:}17{:}11.040$  leads to the development of cancer

NOTE Confidence: 0.76375777

00:17:11.135 --> 00:17:13.785 or contributes to development of

NOTE Confidence: 0.76375777

 $00:17:13.785 \longrightarrow 00:17:16.881$  cancer and the paradigm here is

NOTE Confidence: 0.76375777

 $00:17:16.881 \longrightarrow 00:17:19.387$  is well known where as I said,

NOTE Confidence: 0.76375777

 $00:17:19.390 \longrightarrow 00:17:21.222$  the production of growth.

NOTE Confidence: 0.76375777

00:17:21.222 --> 00:17:23.054 Promoting cytokines combined with

NOTE Confidence: 0.76375777

 $00{:}17{:}23.054 \dashrightarrow 00{:}17{:}25.314$  or radical oxygens that Armenta

NOTE Confidence: 0.76375777

 $00:17:25.314 \longrightarrow 00:17:27.439$  Genic eventually leads to the

NOTE Confidence: 0.76375777

 $00:17:27.439 \longrightarrow 00:17:29.670$  development of cancer angiogenesis.

NOTE Confidence: 0.76375777

 $00:17:29.670 \longrightarrow 00:17:33.126$  Growth stimulation and so on and so forth.

NOTE Confidence: 0.76375777

 $00{:}17{:}33.130 \dashrightarrow 00{:}17{:}36.399$  So the issue is how does salmonella

NOTE Confidence: 0.76375777

00:17:36.399 --> 00:17:38.738 trigger inflammation now on this on?

NOTE Confidence: 0.76375777

 $00:17:38.740 \longrightarrow 00:17:39.994$  On the surface,

NOTE Confidence: 0.76375777

 $00:17:39.994 \longrightarrow 00:17:42.920$  this could be a rather simple story

00:17:43.005 --> 00:17:45.957 and you may know that we are in now

NOTE Confidence: 0.76375777

 $00:17:45.957 \longrightarrow 00:17:48.500$  with innate immune receptors famously

NOTE Confidence: 0.76375777

 $00:17:48.500 \longrightarrow 00:17:52.069$  put into the scientific space by the

NOTE Confidence: 0.76375777

 $00:17:52.069 \longrightarrow 00:17:54.652$  late Charlie Janeway here at Yale and

NOTE Confidence: 0.76375777

 $00{:}17{:}54.652 \dashrightarrow 00{:}17{:}57.543$  this in nate immune receptors have the

NOTE Confidence: 0.76375777

00:17:57.543 --> 00:18:00.138 capacity to recognize bacterial products.

NOTE Confidence: 0.76375777  $00{:}18{:}00.140 \dashrightarrow 00{:}18{:}00.664 \text{ Uh},$ 

NOTE Confidence: 0.76375777

00:18:00.664 --> 00:18:02.760like polysaccharide peptidoglycan flagella.

NOTE Confidence: 0.76375777

00:18:02.760 --> 00:18:04.179 You name it,

NOTE Confidence: 0.76375777

 $00:18:04.179 \longrightarrow 00:18:07.017$  many bacterial products can be detected

NOTE Confidence: 0.76375777

 $00:18:07.017 \longrightarrow 00:18:10.079$  by this innate immune receptors.

NOTE Confidence: 0.76375777

 $00{:}18{:}10.080 \dashrightarrow 00{:}18{:}12.292$  Them essentially coordinate an

NOTE Confidence: 0.76375777

 $00{:}18{:}12.292 \dashrightarrow 00{:}18{:}14.504$  inflammatory response and that

NOTE Confidence: 0.76375777

 $00:18:14.504 \longrightarrow 00:18:16.162$  inflammatory response eventually

NOTE Confidence: 0.76375777

00:18:16.162 --> 00:18:18.592 leads to pathogen rejection and

00:18:18.592 --> 00:18:20.536 they acquired immune response.

NOTE Confidence: 0.76375777

 $00:18:20.540 \longrightarrow 00:18:25.238$  So this is central to the way we hosts,

NOTE Confidence: 0.76375777

 $00:18:25.240 \longrightarrow 00:18:26.890$  not just humans.

NOTE Confidence: 0.76375777

 $00:18:26.890 \longrightarrow 00:18:30.190$  But all mammals defend against microbial.

NOTE Confidence: 0.76375777

 $00:18:30.190 \longrightarrow 00:18:32.479$  Pathogens now it turns out that then

NOTE Confidence: 0.76375777

 $00{:}18{:}32.479 \dashrightarrow 00{:}18{:}34.672$  from these framework it will be very

NOTE Confidence: 0.76375777

 $00:18:34.672 \longrightarrow 00:18:36.394$  simple to think that someone other

NOTE Confidence: 0.858762

00:18:36.456 --> 00:18:37.566 triggers inflammation simply

NOTE Confidence: 0.858762

00:18:37.566 --> 00:18:39.786 because he has plenty of LPS.

NOTE Confidence: 0.858762

 $00:18:39.790 \longrightarrow 00:18:41.608$  He has plenty of these product

NOTE Confidence: 0.858762

 $00:18:41.608 \longrightarrow 00:18:43.621$  and is the detection of the

NOTE Confidence: 0.858762

 $00:18:43.621 \longrightarrow 00:18:45.089$  host that drives inflammation.

NOTE Confidence: 0.858762

 $00:18:45.090 \longrightarrow 00:18:46.059$  In other words,

NOTE Confidence: 0.858762

 $00:18:46.059 \longrightarrow 00:18:48.730$  this will be like a host centric view,

NOTE Confidence: 0.858762

 $00:18:48.730 \longrightarrow 00:18:50.778$  but work that we have done in our

NOTE Confidence: 0.858762

 $00{:}18{:}50.778 \dashrightarrow 00{:}18{:}53.537$  lab for the last 15 years or so has

 $00:18:53.537 \longrightarrow 00:18:55.362$  completely turn around this paradigm

NOTE Confidence: 0.858762

 $00:18:55.362 \longrightarrow 00:18:57.422$  and discovered that that's actually

NOTE Confidence: 0.858762

00:18:57.422 --> 00:18:59.734 incorrect in the case of Salmonella,

NOTE Confidence: 0.858762

 $00:18:59.734 \longrightarrow 00:19:01.166$  that salmonella really has

NOTE Confidence: 0.858762

 $00:19:01.166 \longrightarrow 00:19:02.240$  a specific adaptations.

NOTE Confidence: 0.858762

 $00:19:02.240 \longrightarrow 00:19:04.736$  Evolve by similar to trigger inflammation.

NOTE Confidence: 0.858762

00:19:04.740 --> 00:19:07.659 So this is a pathogen driven process,

NOTE Confidence: 0.858762

 $00:19:07.660 \longrightarrow 00:19:09.750$  not a host driven process,

NOTE Confidence: 0.858762

 $00:19:09.750 \longrightarrow 00:19:12.252$  and the reason is very simple

NOTE Confidence: 0.858762

 $00:19:12.252 \longrightarrow 00:19:13.920$  or not so simple.

NOTE Confidence: 0.858762

00:19:13.920 --> 00:19:16.000 Salmonella, like many other microbes,

NOTE Confidence: 0.858762

 $00:19:16.000 \longrightarrow 00:19:18.496$  when they encounter a mucosal site,

NOTE Confidence: 0.858762

00:19:18.500 --> 00:19:20.168 being an intestinal being

NOTE Confidence: 0.858762

00:19:20.168 --> 00:19:21.419 the Gallbladder mucosa,

NOTE Confidence: 0.858762

 $00:19:21.420 \longrightarrow 00:19:24.048$  they need to compete with resident

 $00:19:24.048 \longrightarrow 00:19:27.002$  microbiota who has a foothold on that

NOTE Confidence: 0.858762

 $00:19:27.002 \longrightarrow 00:19:30.180$  issue and really put up a good fight.

NOTE Confidence: 0.858762

 $00:19:30.180 \longrightarrow 00:19:31.752$  This is actually over.

NOTE Confidence: 0.858762

 $00:19:31.752 \longrightarrow 00:19:33.717$  One of our main barriers

NOTE Confidence: 0.858762

00:19:33.717 --> 00:19:35.609 against bacterial pathogens,

NOTE Confidence: 0.858762

00:19:35.610 --> 00:19:37.254 particularly in this time,

NOTE Confidence: 0.858762

 $00:19:37.254 \longrightarrow 00:19:38.898$  is the resident microbiota.

NOTE Confidence: 0.858762

 $00:19:38.900 \longrightarrow 00:19:40.548$  The inflammatory response crosses

NOTE Confidence: 0.858762

 $00{:}19{:}40.548 {\:\dashrightarrow\:} 00{:}19{:}42.196$  it causes profound dysbiosis,

NOTE Confidence: 0.858762

 $00:19:42.200 \longrightarrow 00:19:44.354$  which is essential for someone else

NOTE Confidence: 0.858762

 $00:19:44.354 \dashrightarrow 00:19:47.550$  to be able to colonize and replicate.

NOTE Confidence: 0.858762

00:19:47.550 --> 00:19:48.786 Not only that,

NOTE Confidence: 0.858762

 $00:19:48.786 \longrightarrow 00:19:50.434$  inflammation makes nutrients available,

NOTE Confidence: 0.858762

 $00:19:50.440 \longrightarrow 00:19:52.236$  electron acceptors camper sourcers

NOTE Confidence: 0.858762

 $00:19:52.236 \longrightarrow 00:19:54.481$  that otherwise would not be

NOTE Confidence: 0.858762

 $00:19:54.481 \longrightarrow 00:19:56.617$  available in the an inflamed tissue,

 $00:19:56.620 \longrightarrow 00:19:58.845$  and that drives the replication

NOTE Confidence: 0.858762

 $00:19:58.845 \longrightarrow 00:20:00.180$  of the aluminum.

NOTE Confidence: 0.858762

00:20:00.180 --> 00:20:02.120 Population of salmon are so,

NOTE Confidence: 0.858762

 $00:20:02.120 \longrightarrow 00:20:04.448$  so is the inflammatory response that

NOTE Confidence: 0.858762

00:20:04.448 --> 00:20:06.486 causes even though someone else

NOTE Confidence: 0.858762

 $00:20:06.486 \longrightarrow 00:20:08.606$  and intracellular pathogen the bulk

NOTE Confidence: 0.858762

00:20:08.606 --> 00:20:10.711 of the bacterial replication comes

NOTE Confidence: 0.858762

 $00{:}20{:}10.711 \dashrightarrow 00{:}20{:}12.739$  from this lumenal population that is

NOTE Confidence: 0.858762

 $00:20:12.739 \longrightarrow 00:20:14.534$  fed from the inflammatory response

NOTE Confidence: 0.858762

 $00:20:14.534 \longrightarrow 00:20:16.856$  triggered by this in this bacteria.

NOTE Confidence: 0.858762

00:20:16.860 --> 00:20:19.576 Here. So a nice division of Labor.

NOTE Confidence: 0.858762

 $00{:}20{:}19.580 \dashrightarrow 00{:}20{:}21.776$  Now how does some one even managed

NOTE Confidence: 0.858762

 $00{:}20{:}21.776 \dashrightarrow 00{:}20{:}23.850$  to trigger an inflammatory response?

NOTE Confidence: 0.858762

 $00:20:23.850 \longrightarrow 00:20:25.850$  Mucosal sites which are actually

NOTE Confidence: 0.858762

00:20:25.850 --> 00:20:27.850 is pretty difficult because mucosal

 $00:20:27.917 \longrightarrow 00:20:30.215$  sites are subject to various stringent

NOTE Confidence: 0.858762

 $00{:}20{:}30.215 \dashrightarrow 00{:}20{:}32.220$  negative regulation of his native.

NOTE Confidence: 0.858762

 $00:20:32.220 \longrightarrow 00:20:34.136$  Respected receptors precisely to

NOTE Confidence: 0.858762

 $00:20:34.136 \longrightarrow 00:20:36.531$  prevent this microbiota that in

NOTE Confidence: 0.858762

00:20:36.531 --> 00:20:39.170 theory can also stimulate in Amy

NOTE Confidence: 0.858762

00:20:39.170 --> 00:20:41.260 receptors to trigger an inflammatory

NOTE Confidence: 0.858762

 $00:20:41.333 \longrightarrow 00:20:43.757$  response and for all of us to be

NOTE Confidence: 0.858762

00:20:43.757 --> 00:20:45.894 working with IBD or Crohn's disease.

NOTE Confidence: 0.858762

 $00{:}20{:}45.894 \longrightarrow 00{:}20{:}48.180$  To avoid that they're very precise

NOTE Confidence: 0.858762

 $00:20:48.253 \longrightarrow 00:20:50.373$  mechanisms to keep those innate

NOTE Confidence: 0.858762

 $00{:}20{:}50.373 \dashrightarrow 00{:}20{:}52.069$  immune receptors in check,

NOTE Confidence: 0.858762

 $00:20:52.070 \longrightarrow 00:20:54.824$  and somebody had to trigger inflammation

NOTE Confidence: 0.858762

 $00:20:54.824 \longrightarrow 00:20:57.739$  in that environment has does he do it?

NOTE Confidence: 0.858762

00:20:57.740 --> 00:20:58.133 Well,

NOTE Confidence: 0.858762

00:20:58.133 --> 00:21:00.491 it does sit through this amazing

NOTE Confidence: 0.858762

 $00{:}21{:}00.491 \dashrightarrow 00{:}21{:}03.054$  machine that Dan alluded earlier that

 $00:21:03.054 \longrightarrow 00:21:06.106$  we discovered more than two decades ago.

NOTE Confidence: 0.858762

 $00{:}21{:}06.110 \dashrightarrow 00{:}21{:}09.470$  It's an amazing sort of bacterial

NOTE Confidence: 0.858762

00:21:09.470 --> 00:21:12.300 injection device if you will.

NOTE Confidence: 0.858762

00:21:12.300 --> 00:21:15.280 That injects bacterially encoded

NOTE Confidence: 0.858762

 $00:21:15.280 \longrightarrow 00:21:16.770$  proteins that.

NOTE Confidence: 0.858762

00:21:16.770 --> 00:21:20.382 Have the capacity to modulate many

NOTE Confidence: 0.858762

00:21:20.382 --> 00:21:22.188 signal transduction pathways.

NOTE Confidence: 0.858762

 $00{:}21{:}22.190 \dashrightarrow 00{:}21{:}24.680$  And it's the ability to stimulate

NOTE Confidence: 0.858762

 $00:21:24.680 \longrightarrow 00:21:26.340$  those signal transduction pathways

NOTE Confidence: 0.858762

 $00:21:26.410 \longrightarrow 00:21:28.275$  and modulate cellular process for

NOTE Confidence: 0.858762

00:21:28.275 --> 00:21:30.140 the benefit of the pathogen

NOTE Confidence: 0.858762

 $00:21:30.203 \longrightarrow 00:21:32.035$  specifically relevant to inflammation

NOTE Confidence: 0.858762

 $00{:}21{:}32.035 \dashrightarrow 00{:}21{:}34.783$  are three of these effective proteins

NOTE Confidence: 0.858762

00:21:34.790 --> 00:21:37.331 that activate Rho Family GT P aces

NOTE Confidence: 0.858762

 $00:21:37.331 \longrightarrow 00:21:39.701$  by either being exchange factors of

00:21:39.701 --> 00:21:42.501 the Pro Family GPs is or forcefully

NOTE Confidence: 0.858762

00:21:42.575 --> 00:21:44.029 nocetti phosphatase.

NOTE Confidence: 0.858762

 $00:21:44.030 \longrightarrow 00:21:46.364$  In the case of this particular

NOTE Confidence: 0.858762

 $00:21:46.364 \longrightarrow 00:21:47.920$  effector that wouldn't activate

NOTE Confidence: 0.858762

00:21:47.987 --> 00:21:50.747 endogenous change factors and activate that,

NOTE Confidence: 0.858762

 $00:21:50.750 \longrightarrow 00:21:54.230$  and that leads to the activation of CDC.

NOTE Confidence: 0.858762

 $00:21:54.230 \longrightarrow 00:21:56.462$  42 and then the activation of CDC 42

NOTE Confidence: 0.858762

 $00:21:56.462 \longrightarrow 00:21:58.079$  leads to transcriptional responses

NOTE Confidence: 0.858762

 $00{:}21{:}58.079 \dashrightarrow 00{:}22{:}00.063$  that really are proinflammatory

NOTE Confidence: 0.858762

 $00:22:00.063 \longrightarrow 00:22:02.047$  and really looked like

NOTE Confidence: 0.8360523

00:22:02.116 --> 00:22:03.109 in 18 responses.

NOTE Confidence: 0.8360523

 $00:22:03.110 \longrightarrow 00:22:05.350$  This was a bit puzzling for a

NOTE Confidence: 0.8360523

00:22:05.350 --> 00:22:07.895 number of years because CDC 42 had

NOTE Confidence: 0.8360523

 $00:22:07.895 \longrightarrow 00:22:10.157$  never been linked to innate immune

NOTE Confidence: 0.8360523

00:22:10.233 --> 00:22:12.369 responses until very recently,

NOTE Confidence: 0.8360523

 $00{:}22{:}12.370 \dashrightarrow 00{:}22{:}14.722$  where we sort of cracked this little

 $00{:}22{:}14.722 \dashrightarrow 00{:}22{:}17.013$  puzzle and we discovered that the

NOTE Confidence: 0.8360523

 $00{:}22{:}17.013 \dashrightarrow 00{:}22{:}19.834$  activation of CDC 42 by Salmonella leads

NOTE Confidence: 0.8360523

 $00:22:19.910 \longrightarrow 00:22:22.334$  to the formation of a noncanonical

NOTE Confidence: 0.8360523

00:22:22.334 --> 00:22:24.618 signaling complex made by pack one.

NOTE Confidence: 0.8360523

00:22:24.618 --> 00:22:26.622 A target of CDC 42 and

NOTE Confidence: 0.8360523

 $00:22:26.622 \longrightarrow 00:22:28.210$  these other components.

NOTE Confidence: 0.8360523

00:22:28.210 --> 00:22:29.226 Trap 6 Tab Tak,

NOTE Confidence: 0.8360523

 $00:22:29.226 \longrightarrow 00:22:32.097$  One Tab 1 Tab 2 that leads to the

NOTE Confidence: 0.8360523

 $00{:}22{:}32.097 \dashrightarrow 00{:}22{:}34.217$  inflammatory response and what is

NOTE Confidence: 0.8360523

00:22:34.217 --> 00:22:36.889 what explains the whole thing is

NOTE Confidence: 0.8360523

 $00{:}22{:}36.889 \rightarrow 00{:}22{:}38.641$  that these signaling complexes

NOTE Confidence: 0.8360523

 $00:22:38.641 \longrightarrow 00:22:40.651$  identical to the signaling complex

NOTE Confidence: 0.8360523

 $00{:}22{:}40.651 \dashrightarrow 00{:}22{:}42.913$  that is tripped by narimi receptors.

NOTE Confidence: 0.8360523

 $00:22:42.920 \longrightarrow 00:22:45.286$  So what someone in essence is doing

NOTE Confidence: 0.8360523

 $00:22:45.286 \longrightarrow 00:22:47.365$  is going down the signaling pathway

 $00:22:47.365 \longrightarrow 00:22:50.285$  so that so as to avoid the negative

NOTE Confidence: 0.8360523

 $00{:}22{:}50.285 \dashrightarrow 00{:}22{:}52.409$  regulatory system and trigger

NOTE Confidence: 0.8360523

 $00:22:52.409 \longrightarrow 00:22:55.064$  essentially an innate immune response.

NOTE Confidence: 0.8360523

00:22:55.070 --> 00:22:57.080 But by non Canonical methods,

NOTE Confidence: 0.8360523

 $00:22:57.080 \longrightarrow 00:22:59.327$  so he uses other type of mechanism

NOTE Confidence: 0.8360523

00:22:59.327 --> 00:23:01.409 similar to this going downstream

NOTE Confidence: 0.8360523

 $00:23:01.409 \longrightarrow 00:23:03.509$  of Canonical signaling pathways.

NOTE Confidence: 0.8360523

00:23:03.510 --> 00:23:06.921 But since my time is up I just gonna

NOTE Confidence: 0.8360523

 $00{:}23{:}06.921 \dashrightarrow 00{:}23{:}10.435$  put up a sort of a summary of these

NOTE Confidence: 0.8360523

 $00:23:10.435 \longrightarrow 00:23:14.286$  and sort of to give you a flavor or

NOTE Confidence: 0.8360523

 $00{:}23{:}14.286 \to 00{:}23{:}17.146$  how these effector proteins can go down.

NOTE Confidence: 0.8360523

 $00{:}23{:}17.146 \dashrightarrow 00{:}23{:}18.328$  Different signaling pathways

NOTE Confidence: 0.8360523

 $00:23:18.328 \longrightarrow 00:23:19.990$  intersect with signaling pathway.

NOTE Confidence: 0.8360523

 $00:23:19.990 \longrightarrow 00:23:22.145$  For example this effector can

NOTE Confidence: 0.8360523

00:23:22.145 --> 00:23:24.879 activate the rig I and MD I5.

NOTE Confidence: 0.8360523

00:23:24.880 --> 00:23:26.556 A nucleotide sensing pathway,

 $00:23:26.556 \longrightarrow 00:23:29.490$  but without the need of nuclear dice.

NOTE Confidence: 0.8360523

 $00{:}23{:}29.490 \dashrightarrow 00{:}23{:}32.166$  It just simply activates regay by

NOTE Confidence: 0.8360523

 $00:23:32.166 \longrightarrow 00:23:34.938$  interfacing with dream 56 and trim 65.

NOTE Confidence: 0.8360523

00:23:34.940 --> 00:23:37.448 Two regulators of this pathway you.

NOTE Confidence: 0.8360523

 $00{:}23{:}37.450 \dashrightarrow 00{:}23{:}40.327$  We could make them activates them and

NOTE Confidence: 0.8360523

 $00:23:40.327 \longrightarrow 00:23:42.897$  trips this signaling pathway without the

NOTE Confidence: 0.8360523

00:23:42.897 --> 00:23:45.830 need of The Agonist of those receptors,

NOTE Confidence: 0.8360523

 $00:23:45.830 \longrightarrow 00:23:47.810$  and the same applies to another

NOTE Confidence: 0.8360523

 $00:23:47.810 \longrightarrow 00:23:49.778$  effector here that it actually

NOTE Confidence: 0.8360523

 $00:23:49.778 \longrightarrow 00:23:52.118$  inhibits an anti-inflammatory pathway.

NOTE Confidence: 0.8360523

00:23:52.120 --> 00:23:55.347 So, but since I don't have time.

NOTE Confidence: 0.8360523

 $00:23:55.350 \longrightarrow 00:23:57.100$  I had to skip it,

NOTE Confidence: 0.8360523

 $00{:}23{:}57.100 \dashrightarrow 00{:}23{:}59.179$  so I hope that you got a sense of

NOTE Confidence: 0.8360523

 $00:23:59.179 \longrightarrow 00:24:01.254$  the sophistication by which bacterial

NOTE Confidence: 0.8360523

 $00:24:01.254 \longrightarrow 00:24:03.918$  pathogens manipulate cells in in ways

 $00:24:03.984 \longrightarrow 00:24:06.546$  that benefit them but doesn't benefit us.

NOTE Confidence: 0.8360523

 $00:24:06.550 \longrightarrow 00:24:08.300$  And through the production of

NOTE Confidence: 0.8360523

00:24:08.300 --> 00:24:09.700 Gina toxins or inflammation,

NOTE Confidence: 0.8360523

 $00:24:09.700 \longrightarrow 00:24:12.234$  it leads to the predisposition to cancer

NOTE Confidence: 0.8360523

00:24:12.234 --> 00:24:14.599 and then finally last but not least,

NOTE Confidence: 0.8360523

00:24:14.600 --> 00:24:17.435 people that were involved in this work

NOTE Confidence: 0.8360523

 $00{:}24{:}17.435 \to 00{:}24{:}19.905$  obviously and talked to work that was

NOTE Confidence: 0.8360523

00:24:19.905 --> 00:24:22.300 done a number of years ago as well,

NOTE Confidence: 0.8360523

00:24:22.300 --> 00:24:25.014 but for the inflammation pathway, who we?

NOTE Confidence: 0.8360523

00:24:25.014 --> 00:24:27.424 Indiana were involved and one

NOTE Confidence: 0.8360523

 $00:24:27.424 \longrightarrow 00:24:30.760$  whose did all this work and Mary,

NOTE Confidence: 0.8360523

 $00:24:30.760 \longrightarrow 00:24:31.708$  of course,

NOTE Confidence: 0.8360523

 $00:24:31.708 \longrightarrow 00:24:34.078$  had made the pioneering discoveries

NOTE Confidence: 0.8360523

 $00:24:34.078 \longrightarrow 00:24:36.749$  of the Genotoxin in Campillo Bacter

NOTE Confidence: 0.8360523

 $00:24:36.749 \longrightarrow 00:24:39.940$  Jejuni and set in motion all this work.

NOTE Confidence: 0.8360523

 $00:24:39.940 \longrightarrow 00:24:42.130$  And thank you very much.

00:24:42.130 --> 00:24:45.178 And with that I'm gonna stop

NOTE Confidence: 0.8360523

 $00:24:45.178 \longrightarrow 00:24:47.210$  sharing if I can.

NOTE Confidence: 0.8360523

 $00:24:47.210 \longrightarrow 00:24:47.980$  And.

NOTE Confidence: 0.7746913

 $00:24:50.600 \longrightarrow 00:24:52.268$  OK, well thank you very much.

NOTE Confidence: 0.7746913

 $00:24:52.270 \longrightarrow 00:24:53.390$  Jorge is very interesting.

NOTE Confidence: 0.7746913

 $00:24:53.390 \longrightarrow 00:24:54.230$  Very exciting work.

NOTE Confidence: 0.7746913

00:24:54.230 --> 00:24:55.866 I don't know how to swim.

NOTE Confidence: 0.7746913

 $00{:}24{:}55.866 \dashrightarrow 00{:}24{:}57.833$  I should know how to stop sharing

NOTE Confidence: 0.7746913

 $00:24:57.833 \longrightarrow 00:24:59.807$  but you help me on that one.

NOTE Confidence: 0.7746913

 $00:24:59.810 \longrightarrow 00:25:01.760$  Yeah, OK.

NOTE Confidence: 0.7746913

 $00:25:01.760 \longrightarrow 00:25:03.260$  If people have questions,

NOTE Confidence: 0.7746913

00:25:03.260 --> 00:25:05.890 you can type them into the chat,

NOTE Confidence: 0.7746913

 $00:25:05.890 \longrightarrow 00:25:07.390$  or Renee's, or way

NOTE Confidence: 0.8369269

 $00:25:07.390 \longrightarrow 00:25:08.509$  to unmute them.

NOTE Confidence: 0.8457918

 $00:25:11.560 \longrightarrow 00:25:12.870$  We can, if you'd like, sure.

 $00:25:14.760 \longrightarrow 00:25:16.522$  I'm ask a quick question.

NOTE Confidence: 0.8003514

 $00:25:16.522 \longrightarrow 00:25:18.852$  I was very struck by that by

NOTE Confidence: 0.8003514

 $00:25:18.852 \longrightarrow 00:25:20.760$  what appears to be the convergent

NOTE Confidence: 0.8003514

 $00:25:20.822 \longrightarrow 00:25:22.877$  evolution of these two nucleases.

NOTE Confidence: 0.8003514

00:25:22.880 --> 00:25:24.640 Yeah, it's really very striking.

NOTE Confidence: 0.8003514

 $00{:}25{:}24.640 \dashrightarrow 00{:}25{:}27.469$  Is there? What is the advantage of the

NOTE Confidence: 0.8003514

00:25:27.470 --> 00:25:30.710 bacteria to induce cell cycle arrest?

NOTE Confidence: 0.8003514

 $00:25:30.710 \longrightarrow 00:25:32.385$  What cell cycle arrest actually

NOTE Confidence: 0.8003514

 $00{:}25{:}32.385 \dashrightarrow 00{:}25{:}33.725$  is also growing flammatory?

NOTE Confidence: 0.8003514

00:25:33.730 --> 00:25:35.760 So probably one of the main drivers

NOTE Confidence: 0.8003514

 $00{:}25{:}35.760 \dashrightarrow 00{:}25{:}37.739$  is the Pro inflammatory response and

NOTE Confidence: 0.8003514

 $00:25:37.739 \longrightarrow 00:25:40.961$  also in the case of some type is using

NOTE Confidence: 0.8003514

 $00:25:40.961 \longrightarrow 00:25:43.139$  this activity to target immune cells.

NOTE Confidence: 0.8003514

00:25:43.140 --> 00:25:45.471 So obviously if you're a virus and

NOTE Confidence: 0.8003514

00:25:45.471 --> 00:25:48.323 you know you you know a thing or two

NOTE Confidence: 0.8003514

 $00:25:48.323 \longrightarrow 00:25:50.336$  about them and you integrate your

00:25:50.336 --> 00:25:52.882 genome in in the host, you're free.

NOTE Confidence: 0.8003514

 $00:25:52.882 \longrightarrow 00:25:53.890$  You know you.

NOTE Confidence: 0.8003514

 $00:25:53.890 \longrightarrow 00:25:55.846$  That's the way you can persist

NOTE Confidence: 0.8003514

 $00:25:55.846 \longrightarrow 00:25:57.590$  as long as you want.

NOTE Confidence: 0.8003514

 $00:25:57.590 \longrightarrow 00:26:00.406$  If you're somebody that I feel you have.

NOTE Confidence: 0.8003514

 $00:26:00.410 \longrightarrow 00:26:02.350$  4761 those are the number

NOTE Confidence: 0.8003514

 $00:26:02.350 \longrightarrow 00:26:03.902$  of open reading frames,

NOTE Confidence: 0.8003514

 $00:26:03.910 \longrightarrow 00:26:06.250$  potential antigens you need to hide.

NOTE Confidence: 0.8003514

00:26:06.250 --> 00:26:08.190 You can't do that right?

NOTE Confidence: 0.8003514

 $00:26:08.190 \longrightarrow 00:26:10.542$  So the way somebody that he does it

NOTE Confidence: 0.8003514

00:26:10.542 --> 00:26:13.633 is by creating a sort of immunological

NOTE Confidence: 0.8003514

00:26:13.633 --> 00:26:15.577 suppression around the site,

NOTE Confidence: 0.8003514

 $00{:}26{:}15.580 \dashrightarrow 00{:}26{:}17.132$  wherein colonizes and these

NOTE Confidence: 0.8003514

 $00:26:17.132 \longrightarrow 00:26:19.072$  toxin is central for that.

NOTE Confidence: 0.8003514

 $00:26:19.080 \longrightarrow 00:26:20.632$  For the persistent infection,

 $00:26:20.632 \longrightarrow 00:26:22.184$  by targeting immune cells.

NOTE Confidence: 0.8003514

 $00:26:22.190 \longrightarrow 00:26:25.310$  So so, and in the case of Campylobacter,

NOTE Confidence: 0.8003514

00:26:25.310 --> 00:26:26.014 of course,

NOTE Confidence: 0.8003514

 $00:26:26.014 \longrightarrow 00:26:28.830$  inflammation is central for the bug and and

NOTE Confidence: 0.8003514

 $00:26:28.905 \longrightarrow 00:26:31.647$  this proinflammatory aspect of DNA damage.

NOTE Confidence: 0.8003514

 $00:26:31.650 \longrightarrow 00:26:33.030$  Is probably what evolutionary

NOTE Confidence: 0.8003514

 $00:26:33.030 \longrightarrow 00:26:34.065$  selected for these,

NOTE Confidence: 0.8003514

 $00:26:34.070 \longrightarrow 00:26:34.762$  you know,

NOTE Confidence: 0.8003514

 $00{:}26{:}34.762 \dashrightarrow 00{:}26{:}36.838$  toxins and the in the process.

NOTE Confidence: 0.8003514

 $00:26:36.840 \longrightarrow 00:26:38.916$  We you know we got clipped.

NOTE Confidence: 0.83454424

 $00:26:40.490 \longrightarrow 00:26:41.710$  Thank you are there

NOTE Confidence: 0.83454424

 $00:26:41.710 \longrightarrow 00:26:43.528$  are there other questions for Jorge?

NOTE Confidence: 0.91647124

00:26:50.550 --> 00:26:52.236 Alright, well thank you very much.

NOTE Confidence: 0.83337504

 $00:26:59.580 \longrightarrow 00:27:03.090$  I think I think Dan froze.

NOTE Confidence: 0.83337504

 $00:27:03.090 \longrightarrow 00:27:05.360$  You were frozen Dan.

NOTE Confidence: 0.83337504

 $00:27:05.360 \longrightarrow 00:27:07.628$  Oh, I'm sorry, frozen.

00:27:09.110 --> 00:27:10.849 I guess introduce you,

NOTE Confidence: 0.8219546

 $00{:}27{:}10.850 \dashrightarrow 00{:}27{:}14.216$  Melinda Kay. Great don't we love

NOTE Confidence: 0.8219546

 $00:27:14.216 \longrightarrow 00:27:16.460$  the advances in technology.

NOTE Confidence: 0.8219546

 $00:27:16.460 \longrightarrow 00:27:19.988$  Thank you Doctor Glenn that was fabulous Ann.

NOTE Confidence: 0.8219546

 $00{:}27{:}19.990 \dashrightarrow 00{:}27{:}22.198$  I am now delighted to introduce

NOTE Confidence: 0.8219546

00:27:22.198 --> 00:27:24.258 Doctor Nicole Diesel to present

NOTE Confidence: 0.8219546

00:27:24.258 --> 00:27:26.314 her research on environmental

NOTE Confidence: 0.8219546

 $00{:}27{:}26.314 \dashrightarrow 00{:}27{:}28.370$  carcinogens and thyroid cancer.

NOTE Confidence: 0.8219546

 $00:27:28.370 \longrightarrow 00:27:30.915$  Doctor Diesel is an associate

NOTE Confidence: 0.8219546

 $00{:}27{:}30.915 \dashrightarrow 00{:}27{:}33.460$  professor of environmental health in

NOTE Confidence: 0.8219546

00:27:33.544 --> 00:27:35.998 the Yale School Public Health and

NOTE Confidence: 0.8219546

 $00{:}27{:}35.998 \dashrightarrow 00{:}27{:}38.950$  she received her pH D in her Masters

NOTE Confidence: 0.8219546

 $00{:}27{:}38.950 \dashrightarrow 00{:}27{:}41.593$  in industrial hygiene from the Johns

NOTE Confidence: 0.8219546

 $00{:}27{:}41.593 \dashrightarrow 00{:}27{:}43.798$  Hopkins School of Public Health.

NOTE Confidence: 0.8219546

 $00:27:43.800 \longrightarrow 00:27:45.548$  Her environmental exposure assessment

 $00:27:45.548 \longrightarrow 00:27:47.733$  strategies aimed to reduce exposure

NOTE Confidence: 0.8219546

 $00:27:47.733 \longrightarrow 00:27:49.190$  misclassification for epidemiological.

NOTE Confidence: 0.8219546

 $00:27:49.190 \longrightarrow 00:27:51.425$  Studies and in advance understanding

NOTE Confidence: 0.8219546

 $00:27:51.425 \longrightarrow 00:27:53.660$  of the relationship between exposure

NOTE Confidence: 0.8219546

 $00:27:53.726 \longrightarrow 00:27:54.920$  to environmental environmental

NOTE Confidence: 0.8219546

 $00:27:54.920 \longrightarrow 00:27:57.308$  chemicals in the risk of cancer

NOTE Confidence: 0.8219546

00:27:57.308 --> 00:27:59.607 in other adverse health outcomes,

NOTE Confidence: 0.8219546

00:27:59.610 --> 00:28:02.346 she serves as the Pi of a study funded

NOTE Confidence: 0.8219546

 $00{:}28{:}02.346 \dashrightarrow 00{:}28{:}05.506$  by the American Cancer Society and

NOTE Confidence: 0.8219546

00:28:05.506 --> 00:28:08.286 investigating exposure to flame retardants,

NOTE Confidence: 0.8219546

00:28:08.290 --> 00:28:08.750 pesticides,

NOTE Confidence: 0.8219546

 $00:28:08.750 \longrightarrow 00:28:11.050$  and other persistent pollutants in

NOTE Confidence: 0.8219546

00:28:11.050 --> 00:28:13.489 thyroid cancer risk and of note,

NOTE Confidence: 0.8219546

 $00:28:13.490 \longrightarrow 00:28:16.522$  she is the winner of the Yale Cancer

NOTE Confidence: 0.8219546

00:28:16.522 --> 00:28:19.648 Center 2020 Research Prize in population.

NOTE Confidence: 0.8219546

00:28:19.650 --> 00:28:22.226 Science for her research on this topic,

 $00:28:22.230 \longrightarrow 00:28:24.450$  so we're delighted for your presentation.

NOTE Confidence: 0.8219546

 $00:28:24.450 \longrightarrow 00:28:25.186$  Doctor diesel.

NOTE Confidence: 0.8219546

 $00:28:25.186 \longrightarrow 00:28:26.290$  Take it away.

NOTE Confidence: 0.8562479

00:28:27.930 --> 00:28:30.450 OK, thank you so much Melinda

NOTE Confidence: 0.8562479

 $00:28:30.450 \longrightarrow 00:28:32.130$  for the generous introduction.

NOTE Confidence: 0.8562479

 $00:28:32.130 \longrightarrow 00:28:34.853$  Very pleased to be here to share

NOTE Confidence: 0.8562479

 $00:28:34.853 \longrightarrow 00:28:38.010$  some of my recent work with you.

NOTE Confidence: 0.8562479

 $00:28:38.010 \longrightarrow 00:28:40.374$  I really enjoyed Doctor Galanes presentation

NOTE Confidence: 0.8562479

 $00:28:40.374 \longrightarrow 00:28:42.470$  looking at exposure to microbial

NOTE Confidence: 0.8562479

 $00:28:42.470 \longrightarrow 00:28:44.730$  pathogens and the associated toxins,

NOTE Confidence: 0.8562479

 $00{:}28{:}44.730 \dashrightarrow 00{:}28{:}47.628$  and I'll be switching gears a little

NOTE Confidence: 0.8562479

 $00:28:47.628 \longrightarrow 00:28:51.544$  bit to look at work looking at the

NOTE Confidence: 0.8562479

 $00{:}28{:}51.544 \dashrightarrow 00{:}28{:}54.129$  Epidemiology of exposures to chemical

NOTE Confidence: 0.8562479

 $00{:}28{:}54.224 \dashrightarrow 00{:}28{:}56.899$  toxins and thyroid cancer risk.

NOTE Confidence: 0.8562479

00:28:56.900 --> 00:29:00.276 OK, so I've advanced my slide and someone

 $00:29:00.276 \longrightarrow 00:29:04.229$  can let me know if there's any issue there.

NOTE Confidence: 0.8562479

 $00{:}29{:}04.230 \dashrightarrow 00{:}29{:}06.934$  I first wanted to take a moment just

NOTE Confidence: 0.8562479

 $00:29:06.934 \longrightarrow 00:29:09.848$  to tell you about the motivation of

NOTE Confidence: 0.8562479

 $00:29:09.848 \longrightarrow 00:29:12.588$  my research and the research I'll

NOTE Confidence: 0.8562479

 $00:29:12.588 \longrightarrow 00:29:15.636$  be presenting today and talk about

NOTE Confidence: 0.8562479

 $00:29:15.636 \longrightarrow 00:29:17.962$  environmental risk factors for cancer.

NOTE Confidence: 0.8562479

 $00:29:17.962 \longrightarrow 00:29:20.769$  We know that third of cancers are

NOTE Confidence: 0.8562479

 $00:29:20.769 \longrightarrow 00:29:22.760$  attributable to modifiable factors.

NOTE Confidence: 0.8562479

 $00{:}29{:}22.760 \longrightarrow 00{:}29{:}26.208$  We often think of things related to diet,

NOTE Confidence: 0.8562479

00:29:26.210 --> 00:29:27.150 alcohol, tobacco,

NOTE Confidence: 0.8562479

 $00:29:27.150 \longrightarrow 00:29:29.030$  these so-called lifestyle factors.

NOTE Confidence: 0.8562479

 $00:29:29.030 \longrightarrow 00:29:32.114$  But this also includes infections which

NOTE Confidence: 0.8562479

00:29:32.114 --> 00:29:36.088 we just heard about as well as pollution.

NOTE Confidence: 0.8562479

 $00:29:36.090 \longrightarrow 00:29:39.240$  So how much of cancer cases can

NOTE Confidence: 0.8562479

 $00:29:39.240 \longrightarrow 00:29:42.130$  we attribute to this pollution?

NOTE Confidence: 0.8562479

00:29:42.130 --> 00:29:46.282 While a doll and Peto in their landmark

 $00{:}29{:}46.282 \dashrightarrow 00{:}29{:}49.689$  study estimated about 7% of cancer deaths

NOTE Confidence: 0.8562479

00:29:49.689 --> 00:29:52.204 could be attributable to occupation,

NOTE Confidence: 0.8562479

00:29:52.210 --> 00:29:54.230 pollution and industrial products,

NOTE Confidence: 0.8562479

 $00:29:54.230 \longrightarrow 00:29:57.260$  in many experts agree that this

NOTE Confidence: 0.8562479

00:29:57.340 --> 00:29:59.560 percentage is likely grossly.

NOTE Confidence: 0.8562479

00:29:59.560 --> 00:30:02.500 Under arrest Maded due to the extremely

NOTE Confidence: 0.8562479

 $00:30:02.500 \longrightarrow 00:30:05.380$  limited data on the commercial chemicals

NOTE Confidence: 0.8562479

 $00:30:05.380 \longrightarrow 00:30:08.964$  that we encounter in our day-to-day lives.

NOTE Confidence: 0.8562479

 $00:30:08.970 \longrightarrow 00:30:11.688$  So in the United States there

NOTE Confidence: 0.8562479

 $00:30:11.688 \longrightarrow 00:30:14.118$  are 80,000 chemicals that are

NOTE Confidence: 0.8562479

00:30:14.118 --> 00:30:16.230 licensed for commercial use,

NOTE Confidence: 0.8562479

 $00:30:16.230 \longrightarrow 00:30:18.650$  and of those only 200.

NOTE Confidence: 0.8562479

 $00{:}30{:}18.650 \dashrightarrow 00{:}30{:}22.124$  So not even a percentage of them have been

NOTE Confidence: 0.8562479

 $00:30:22.124 \longrightarrow 00:30:24.940$  screened adequately for carcinogenicity.

NOTE Confidence: 0.8562479

00:30:24.940 --> 00:30:28.328 And every time I share this statistic,

 $00:30:28.330 \longrightarrow 00:30:32.170$  I find it really striking.

NOTE Confidence: 0.8562479

 $00:30:32.170 \longrightarrow 00:30:34.844$  Another reason why this is so important

NOTE Confidence: 0.8562479

 $00:30:34.844 \longrightarrow 00:30:38.570$  is that you know many of these exposures

NOTE Confidence: 0.8562479

 $00:30:38.570 \longrightarrow 00:30:40.570$  are outside individual control.

NOTE Confidence: 0.8562479

 $00:30:40.570 \longrightarrow 00:30:43.222$  These are things in air pollution

NOTE Confidence: 0.8562479

 $00:30:43.222 \longrightarrow 00:30:44.548$  or water supply,

NOTE Confidence: 0.8562479

 $00:30:44.550 \longrightarrow 00:30:45.876$  the food supply,

NOTE Confidence: 0.8562479

00:30:45.876 --> 00:30:46.760 our workplaces,

NOTE Confidence: 0.8562479

 $00:30:46.760 \longrightarrow 00:30:49.224$  so we really rely on the government

NOTE Confidence: 0.8562479

 $00:30:49.224 \longrightarrow 00:30:52.402$  to protect us from exposure to these

NOTE Confidence: 0.8562479

 $00{:}30{:}52.402 \dashrightarrow 00{:}30{:}54.446$  potentially harmful chemicals and

NOTE Confidence: 0.8562479

 $00:30:54.446 \longrightarrow 00:30:57.328$  our regulatory system really is quite

NOTE Confidence: 0.8562479

 $00:30:57.328 \longrightarrow 00:30:59.563$  inadequate to serve this purpose.

NOTE Confidence: 0.8562479

 $00:30:59.570 \longrightarrow 00:31:01.666$  The way it's structured.

NOTE Confidence: 0.8562479

 $00:31:01.666 \longrightarrow 00:31:04.810$  Chemicals have to be proven harmful

NOTE Confidence: 0.8562479

00:31:04.900 --> 00:31:08.218 rather than proven safe at the outset,

 $00:31:08.220 \longrightarrow 00:31:10.665$  so it normally requires researchers

NOTE Confidence: 0.8562479

 $00:31:10.665 \longrightarrow 00:31:14.567$  like myself and others in my fields who

NOTE Confidence: 0.8562479

 $00:31:14.567 \longrightarrow 00:31:17.309$  study chemicals you know for decades

NOTE Confidence: 0.8562479

00:31:17.309 --> 00:31:20.696 before we acquire enough evidence to

NOTE Confidence: 0.8562479

 $00:31:20.696 \longrightarrow 00:31:23.541$  demonstrate harm for particular chemical.

NOTE Confidence: 0.8562479

 $00:31:23.550 \longrightarrow 00:31:24.963$  And also importantly,

NOTE Confidence: 0.8562479

 $00:31:24.963 \longrightarrow 00:31:27.789$  we know these exposures are not

NOTE Confidence: 0.8562479

 $00:31:27.789 \longrightarrow 00:31:29.549$  distributed equitably across

NOTE Confidence: 0.8562479

 $00{:}31{:}29.549 \dashrightarrow 00{:}31{:}31.965$  populations and that populations.

NOTE Confidence: 0.8562479

 $00:31:31.970 \longrightarrow 00:31:34.022$  Experiencing other social disadvantages

NOTE Confidence: 0.8562479

 $00:31:34.022 \longrightarrow 00:31:35.561$  are often disproportionately

NOTE Confidence: 0.8562479

00:31:35.561 --> 00:31:37.810 exposed to certain pollutants,

NOTE Confidence: 0.8562479

 $00:31:37.810 \longrightarrow 00:31:41.344$  and some of these points are

NOTE Confidence: 0.8562479

 $00:31:41.344 \longrightarrow 00:31:44.364$  highlighted in a forthcoming book

NOTE Confidence: 0.8562479

 $00{:}31{:}44.364 \dashrightarrow 00{:}31{:}48.270$  chapter that I worked on with Doctor

00:31:48.270 --> 00:31:51.250 Orwin edited by Charlie Fuchs.

NOTE Confidence: 0.8562479

 $00{:}31{:}51.250 \dashrightarrow 00{:}31{:}53.686$  So turning to the specific research

NOTE Confidence: 0.8562479

00:31:53.686 --> 00:31:56.369 I want to talk about today,

NOTE Confidence: 0.8562479

 $00:31:56.370 \longrightarrow 00:31:58.938$  which is related to thyroid cancer,

NOTE Confidence: 0.8562479

 $00:31:58.940 \longrightarrow 00:32:01.929$  thyroid cancer is the one of the

NOTE Confidence: 0.8562479

 $00:32:01.929 \longrightarrow 00:32:03.210$  fastest growing malignancy's.

NOTE Confidence: 0.8562479

 $00:32:03.210 \longrightarrow 00:32:05.766$  It has nearly tripled over the

NOTE Confidence: 0.8562479

 $00:32:05.766 \longrightarrow 00:32:07.044$  past few decades.

NOTE Confidence: 0.8562479

 $00{:}32{:}07.050 \longrightarrow 00{:}32{:}10.046$  As you can see in these graphs

NOTE Confidence: 0.8562479

 $00{:}32{:}10.046 \dashrightarrow 00{:}32{:}12.859$  of SEER cancer incidence data.

NOTE Confidence: 0.8562479

 $00{:}32{:}12.860 \dashrightarrow 00{:}32{:}16.644$  You can also know by looking at the

NOTE Confidence: 0.8562479

 $00:32:16.644 \longrightarrow 00:32:21.204 \text{ Y}$  axis that females have three times

NOTE Confidence: 0.8562479

 $00:32:21.204 \longrightarrow 00:32:24.699$  the incidence compared to males.

NOTE Confidence: 0.8562479

00:32:24.700 --> 00:32:27.640 Can thyroid cancer, you know,

NOTE Confidence: 0.8562479

 $00:32:27.640 \longrightarrow 00:32:30.570$  has a very good prognosis.

NOTE Confidence: 0.84964806

 $00:32:30.570 \longrightarrow 00:32:35.266$  It's more than 90% survival after 20 years.

00:32:35.270 --> 00:32:38.890 However, survivors face many. Physical,

NOTE Confidence: 0.84964806

 $00:32:38.890 \longrightarrow 00:32:41.910$  psychological and financial challenges.

NOTE Confidence: 0.84964806

00:32:41.910 --> 00:32:44.930 With the prolonged treatments,

NOTE Confidence: 0.84964806

00:32:44.930 --> 00:32:50.312 increased surveillance risk of second primary

NOTE Confidence: 0.84964806

 $00{:}32{:}50.312 \dashrightarrow 00{:}32{:}55.959$  cancer and other quality of life issues.

NOTE Confidence: 0.84964806

 $00:32:55.960 \longrightarrow 00:32:59.152$  So this increase is likely certainly

NOTE Confidence: 0.84964806

 $00:32:59.152 \longrightarrow 00:33:03.610$  due at least in part to improvements

NOTE Confidence: 0.84964806

00:33:03.610 --> 00:33:07.320 and changes to diagnostic techniques,

NOTE Confidence: 0.84964806

 $00:33:07.320 \longrightarrow 00:33:09.213$  imaging techniques and

NOTE Confidence: 0.84964806

 $00:33:09.213 \longrightarrow 00:33:11.737$  an fine needle biopsy's.

NOTE Confidence: 0.84964806

 $00:33:11.740 \longrightarrow 00:33:15.220$  So there's some debate about what

NOTE Confidence: 0.84964806

 $00{:}33{:}15.220 \dashrightarrow 00{:}33{:}18.352$  proportion can be attributed to

NOTE Confidence: 0.84964806

 $00{:}33{:}18.352 \dashrightarrow 00{:}33{:}21.196$  this increased diagnostic scrutiny,

NOTE Confidence: 0.84964806

00:33:21.200 --> 00:33:24.485 but many analysis suggests that

NOTE Confidence: 0.84964806

 $00:33:24.485 \longrightarrow 00:33:27.113$  about half of this.

 $00:33:27.120 \longrightarrow 00:33:31.350$  Trend can be linked to

NOTE Confidence: 0.84964806

00:33:31.350 --> 00:33:33.888 these diagnostic changes,

NOTE Confidence: 0.84964806

 $00:33:33.890 \longrightarrow 00:33:37.270$  leaving half for environmental

NOTE Confidence: 0.84964806

 $00:33:37.270 \longrightarrow 00:33:39.805$  or lifestyle factors.

NOTE Confidence: 0.8233529

00:33:44.950 --> 00:33:47.830 I'm so we've hypothesized that increasing

NOTE Confidence: 0.8233529

 $00:33:47.830 \longrightarrow 00:33:50.405$  exposure to thyroid hormone disrupting

NOTE Confidence: 0.8233529

 $00{:}33{:}50.405 \dashrightarrow 00{:}33{:}53.325$  environmental chemicals such as these

NOTE Confidence: 0.8233529

 $00:33:53.325 \longrightarrow 00:33:55.661$  polybrominated diphenyl ether flame

NOTE Confidence: 0.8233529

00:33:55.735 --> 00:33:58.703 retardants or PVD ES may be partially

NOTE Confidence: 0.8233529

 $00:33:58.703 \longrightarrow 00:34:00.445$  driving this increasing trend.

NOTE Confidence: 0.8233529

 $00:34:00.445 \longrightarrow 00:34:03.235$  So I'll just talk a little

NOTE Confidence: 0.8233529

 $00:34:03.235 \longrightarrow 00:34:05.990$  bit more about these people.

NOTE Confidence: 0.8233529

 $00:34:05.990 \longrightarrow 00:34:10.064$  These are actually a lot of thyroid

NOTE Confidence: 0.8233529

 $00:34:10.064 \longrightarrow 00:34:11.810$  hormone disrupting environmental

NOTE Confidence: 0.8233529

 $00:34:11.900 \longrightarrow 00:34:15.239$  chemicals in use an in the environment.

NOTE Confidence: 0.8233529

 $00:34:15.240 \longrightarrow 00:34:18.246$  These flame retardants were widely added.

 $00:34:18.250 \longrightarrow 00:34:20.330$  Too many different products.

NOTE Confidence: 0.8233529

 $00{:}34{:}20.330 \to 00{:}34{:}23.450$  The polyure thane foam in mattress is

NOTE Confidence: 0.8233529

00:34:23.539 --> 00:34:26.264 an couch, cushions and vehicle seats,

NOTE Confidence: 0.8233529

 $00:34:26.264 \longrightarrow 00:34:28.268$  including baby car seats.

NOTE Confidence: 0.8233529

 $00{:}34{:}28.270 \dashrightarrow 00{:}34{:}31.270$  They were also added to electronics

NOTE Confidence: 0.8233529

 $00{:}34{:}31.270 \dashrightarrow 00{:}34{:}33.932$  like phones, cell phones, televisions,

NOTE Confidence: 0.8233529

 $00:34:33.932 \longrightarrow 00:34:37.256$  computers and the reason they were

NOTE Confidence: 0.8233529

 $00:34:37.256 \longrightarrow 00:34:40.210$  added was to meet a flammability

NOTE Confidence: 0.8233529

00:34:40.210 --> 00:34:43.088 standards such that if these products

NOTE Confidence: 0.8233529

 $00:34:43.088 \longrightarrow 00:34:46.469$  you know caught fire they would burn.

NOTE Confidence: 0.8233529

 $00:34:46.470 \longrightarrow 00:34:47.316$  More slowly,

NOTE Confidence: 0.8233529

 $00{:}34{:}47.316 \dashrightarrow 00{:}34{:}50.277$  which is a good thing from a

NOTE Confidence: 0.8233529

 $00:34:50.277 \longrightarrow 00:34:52.470$  public health perspective.

NOTE Confidence: 0.8233529

00:34:52.470 --> 00:34:52.970 However,

NOTE Confidence: 0.8233529

 $00:34:52.970 \longrightarrow 00:34:56.470$  these chemicals once added to these products,

 $00:34:56.470 \longrightarrow 00:35:00.382$  did not stay bound in the matrices as

NOTE Confidence: 0.8233529

 $00:35:00.382 \dashrightarrow 00:35:03.368$  indicated by their manufacturers and

NOTE Confidence: 0.8233529

 $00:35:03.368 \longrightarrow 00:35:07.820$  instead have migrated out into our homes.

NOTE Confidence: 0.8233529

 $00:35:07.820 \longrightarrow 00:35:09.748$  At home environments, cars,

NOTE Confidence: 0.8233529

 $00:35:09.748 \longrightarrow 00:35:10.613$  workplaces, etc.

NOTE Confidence: 0.8233529

 $00:35:10.613 \longrightarrow 00:35:12.911$  So due to this widespread use

NOTE Confidence: 0.8233529

 $00:35:12.911 \longrightarrow 00:35:15.981$  as well as disposal and improper

NOTE Confidence: 0.8233529

 $00:35:15.981 \longrightarrow 00:35:18.417$  disposal of these chemicals,

NOTE Confidence: 0.8233529

 $00{:}35{:}18.420 \to 00{:}35{:}21.312$  they aren't ubiquitous and more than

NOTE Confidence: 0.8233529

 $00:35:21.312 \longrightarrow 00:35:26.136$  90% of the population here in the US and

NOTE Confidence: 0.8233529

 $00{:}35{:}26.136 \to 00{:}35{:}30.320$  globally are exposed to these chemicals.

NOTE Confidence: 0.8233529

 $00:35:30.320 \longrightarrow 00:35:34.324$  And this also they are extremely persistent

NOTE Confidence: 0.8233529

00:35:34.324 --> 00:35:39.260 once they get into their homes or our bodies,

NOTE Confidence: 0.8233529

 $00:35:39.260 \longrightarrow 00:35:42.620$  they do not degrade very easily,

NOTE Confidence: 0.8233529

 $00:35:42.620 \longrightarrow 00:35:47.084$  so they stick around for years and decades.

NOTE Confidence: 0.8233529

 $00:35:47.090 \longrightarrow 00:35:50.444$  So due to concerns about this

 $00:35:50.444 \longrightarrow 00:35:52.680$  persistence and potential toxicities,

NOTE Confidence: 0.8233529

 $00:35:52.680 \longrightarrow 00:35:55.480$  these particular group of chemicals,

NOTE Confidence: 0.8233529

 $00:35:55.480 \longrightarrow 00:35:58.505$  the PDE's were phase outs

NOTE Confidence: 0.8233529

 $00:35:58.505 \longrightarrow 00:36:01.530$  were initiated over the last.

NOTE Confidence: 0.8233529

00:36:01.530 --> 00:36:02.859 Past decade, however,

NOTE Confidence: 0.8233529

 $00:36:02.859 \longrightarrow 00:36:04.631$  exposures do continue for

NOTE Confidence: 0.8233529

 $00:36:04.631 \longrightarrow 00:36:06.770$  the reasons I described.

NOTE Confidence: 0.8233529

 $00:36:06.770 \longrightarrow 00:36:08.016$  Their persistence,

NOTE Confidence: 0.8233529

00:36:08.016 --> 00:36:09.262 you know,

NOTE Confidence: 0.8233529

 $00:36:09.262 \longrightarrow 00:36:13.560$  their presence in products made before then.

NOTE Confidence: 0.8233529

 $00:36:13.560 \longrightarrow 00:36:16.104$  As well as their presence in

NOTE Confidence: 0.8233529

00:36:16.104 --> 00:36:18.780 the food supply and elsewhere.

NOTE Confidence: 0.8233529

 $00:36:18.780 \longrightarrow 00:36:21.066$  One other group of chemicals that

NOTE Confidence: 0.8233529

 $00:36:21.066 \longrightarrow 00:36:24.126$  will be talking about today are the

NOTE Confidence: 0.8233529

 $00:36:24.126 \longrightarrow 00:36:26.070$  polychlorinated biphenyls or PCB's.

 $00:36:26.070 \longrightarrow 00:36:28.220$  These were also used widely

NOTE Confidence: 0.8233529

 $00{:}36{:}28.220 --> 00{:}36{:}29.510 \ \mathrm{in \ electrical \ equipment},$ 

NOTE Confidence: 0.8233529

 $00:36:29.510 \longrightarrow 00:36:31.222$  hydraulic machinery construction materials.

NOTE Confidence: 0.8233529

 $00:36:31.222 \longrightarrow 00:36:33.362$  These were banned in 1979,

NOTE Confidence: 0.8233529

00:36:33.370 --> 00:36:35.938 so again, you might say why?

NOTE Confidence: 0.8233529

 $00:36:35.940 \longrightarrow 00:36:38.936$  Why are we even studying these now?

NOTE Confidence: 0.8233529

 $00:36:38.940 \longrightarrow 00:36:39.366$  Well,

NOTE Confidence: 0.8233529

 $00:36:39.366 \longrightarrow 00:36:41.496$  there's still around and they're

NOTE Confidence: 0.8233529

 $00:36:41.496 \longrightarrow 00:36:44.089$  still around in our our bodies.

NOTE Confidence: 0.8233529

00:36:44.090 --> 00:36:46.240 Our bloodstreams in the environment,

NOTE Confidence: 0.8233529

 $00{:}36{:}46.240 \dashrightarrow 00{:}36{:}48.778$  and in fact here in Connecticut

NOTE Confidence: 0.8233529

 $00:36:48.778 \longrightarrow 00:36:51.093$  there's been some renewed concern

NOTE Confidence: 0.8233529

 $00:36:51.093 \longrightarrow 00:36:53.289$  about these legacy chemicals.

NOTE Confidence: 0.8233529

00:36:53.290 --> 00:36:56.038 They were commonly used in buildings,

NOTE Confidence: 0.8233529

 $00:36:56.040 \longrightarrow 00:36:57.420$  including schools constructed

NOTE Confidence: 0.8233529

 $00:36:57.420 \longrightarrow 00:36:59.720$  in the 1950s to 1970s,

 $00:36:59.720 \longrightarrow 00:37:02.380$  and many of these schools now are

NOTE Confidence: 0.8233529

 $00:37:02.380 \longrightarrow 00:37:05.680$  in need of repairs and renovations,

NOTE Confidence: 0.8233529

 $00{:}37{:}05.680 \dashrightarrow 00{:}37{:}08.410$  and there have been some notable

NOTE Confidence: 0.8233529

 $00:37:08.410 \longrightarrow 00:37:11.215$  schools in Connecticut that I've had

NOTE Confidence: 0.8233529

 $00{:}37{:}11.215 \dashrightarrow 00{:}37{:}13.490$  PCB levels exceeding safe levels.

NOTE Confidence: 0.8233529

00:37:13.490 --> 00:37:15.780 Closures of schools you know,

NOTE Confidence: 0.8233529

 $00:37:15.780 \longrightarrow 00:37:18.234$  insufficient funds to do a proper

NOTE Confidence: 0.8233529

 $00:37:18.234 \longrightarrow 00:37:20.830$  and safe remodeling or renovations,

NOTE Confidence: 0.8233529

 $00:37:20.830 \longrightarrow 00:37:23.668$  and again, often these are in.

NOTE Confidence: 0.8233529

 $00:37:23.670 \longrightarrow 00:37:27.740$  Kind of environmental justice communities.

NOTE Confidence: 0.8233529

 $00:37:27.740 \longrightarrow 00:37:31.114$  So another reason to study these legacy

NOTE Confidence: 0.8233529

 $00:37:31.114 \longrightarrow 00:37:34.399$  chemicals is as they get phased out,

NOTE Confidence: 0.8233529

 $00{:}37{:}34.400 \dashrightarrow 00{:}37{:}37.739$  new chemicals come to take their place,

NOTE Confidence: 0.8233529

 $00:37:37.740 \longrightarrow 00:37:41.268$  and many of those are also also have

NOTE Confidence: 0.8233529

 $00:37:41.268 \longrightarrow 00:37:43.918$  similar properties and so understanding.

 $00:37:43.920 \longrightarrow 00:37:46.764$  These may help us inform greener

NOTE Confidence: 0.8233529

00:37:46.764 --> 00:37:48.660 chemistry or future regulations

NOTE Confidence: 0.8233529

 $00:37:48.737 \longrightarrow 00:37:50.589$  of other other chemicals.

NOTE Confidence: 0.84945095

 $00:37:54.200 \longrightarrow 00:37:56.666$  So we hypothesize that these PV

NOTE Confidence: 0.84945095

 $00:37:56.666 \longrightarrow 00:37:59.252$  East could be contributing to that

NOTE Confidence: 0.84945095

 $00{:}37{:}59.252 \dashrightarrow 00{:}38{:}01.427$  increasing trend in thy roid cancer.

NOTE Confidence: 0.84945095

 $00:38:01.430 \longrightarrow 00:38:04.587$  Here is a graph showing increasing exposure

NOTE Confidence: 0.84945095

 $00:38:04.587 \longrightarrow 00:38:08.127$  over a similar time period where we saw

NOTE Confidence: 0.84945095

 $00{:}38{:}08.127 \dashrightarrow 00{:}38{:}10.780$  thyroid cancer cases start to go up.

NOTE Confidence: 0.84945095

 $00:38:10.780 \longrightarrow 00:38:13.727$  So these are measurements taken from blood

NOTE Confidence: 0.84945095

 $00:38:13.727 \longrightarrow 00:38:16.933$  samples from a blood bank. In the US.

NOTE Confidence: 0.84945095

00:38:16.933 --> 00:38:20.009 You can see about a doubling every five

NOTE Confidence: 0.84945095

 $00:38:20.009 \longrightarrow 00:38:22.679$  years of these particular chemicals.

NOTE Confidence: 0.79974365

00:38:24.870 --> 00:38:27.630 So looking at more recent data,

NOTE Confidence: 0.79974365

 $00:38:27.630 \longrightarrow 00:38:29.470 I$ , as I mentioned,

NOTE Confidence: 0.79974365

 $00:38:29.470 \longrightarrow 00:38:32.230$  these have been somewhat phased out.

 $00:38:32.230 \longrightarrow 00:38:34.804$  You can see that well levels

NOTE Confidence: 0.79974365

 $00:38:34.804 \longrightarrow 00:38:37.107$  have come down since those

NOTE Confidence: 0.79974365

 $00:38:37.107 \longrightarrow 00:38:39.587$  some of those earlier years,

NOTE Confidence: 0.79974365

 $00:38:39.590 \longrightarrow 00:38:42.810$  but then they really have somewhat plateaued.

NOTE Confidence: 0.79974365

00:38:42.810 --> 00:38:45.570 Or are, you know some some

NOTE Confidence: 0.79974365

00:38:45.570 --> 00:38:47.410 particular congeners of these?

NOTE Confidence: 0.79974365

 $00:38:47.410 \longrightarrow 00:38:50.980$  In this family of chemicals are still

NOTE Confidence: 0.79974365

 $00{:}38{:}50.980 \dashrightarrow 00{:}38{:}53.878$  increasing slightly an we see similar.

NOTE Confidence: 0.79974365

 $00:38:53.880 \longrightarrow 00:38:56.040$  Trends with the PCB's that levels

NOTE Confidence: 0.79974365

00:38:56.040 --> 00:38:58.688 have come down since they were banned,

NOTE Confidence: 0.79974365

 $00{:}38{:}58.690 \dashrightarrow 00{:}39{:}01.168$  but then they reached this plateau

NOTE Confidence: 0.79974365

00:39:01.168 --> 00:39:03.640 in the population because of their

NOTE Confidence: 0.79974365

 $00{:}39{:}03.640 \dashrightarrow 00{:}39{:}05.872$  persistence and then as new chemicals

NOTE Confidence: 0.79974365

 $00:39:05.872 \longrightarrow 00:39:08.238$  come on we may be introduced to

NOTE Confidence: 0.79974365

 $00:39:08.238 \longrightarrow 00:39:10.160$  those on top of these exposures.

 $00:39:12.440 \longrightarrow 00:39:13.976$  Hey and so why?

NOTE Confidence: 0.81618255

 $00:39:13.976 \longrightarrow 00:39:16.280$  Why do we think these may

NOTE Confidence: 0.81618255

 $00:39:16.382 \longrightarrow 00:39:19.007$  be linked to thyroid cancer?

NOTE Confidence: 0.81618255

00:39:19.010 --> 00:39:20.762 These chemicals are established

NOTE Confidence: 0.81618255

00:39:20.762 --> 00:39:22.076 thyroid hormone disruptors.

NOTE Confidence: 0.81618255

00:39:22.080 --> 00:39:23.840 Their endocrine disruptors and

NOTE Confidence: 0.81618255

 $00{:}39{:}23.840 \dashrightarrow 00{:}39{:}27.429$  over here I have an image of our

NOTE Confidence: 0.81618255

00:39:27.429 --> 00:39:29.589 thyroid hormone thyroxine and then

NOTE Confidence: 0.81618255

 $00:39:29.589 \longrightarrow 00:39:33.091$  the PCB's and the PVD ES and their

NOTE Confidence: 0.81618255

 $00:39:33.091 \longrightarrow 00:39:35.211$  general chemical structure so you

NOTE Confidence: 0.81618255

 $00:39:35.220 \longrightarrow 00:39:37.405$  can see immediately how structurally

NOTE Confidence: 0.81618255

 $00:39:37.405 \longrightarrow 00:39:39.153$  similar these chemicals are.

NOTE Confidence: 0.81618255

 $00:39:39.160 \longrightarrow 00:39:42.345$  Shut thyrax, and we've got the two.

NOTE Confidence: 0.81618255

 $00:39:42.350 \longrightarrow 00:39:44.278$  Aromatic rings and then

NOTE Confidence: 0.81618255

 $00:39:44.278 \longrightarrow 00:39:46.206$  while thyroxine has iodine,

NOTE Confidence: 0.81618255

 $00:39:46.210 \dashrightarrow 00:39:48.630$  these chemicals have other halogens.

 $00:39:48.630 \longrightarrow 00:39:51.528$  They have either chlorine or bromine's.

NOTE Confidence: 0.81618255

00:39:51.530 --> 00:39:54.230 Just to further illustrate when for

NOTE Confidence: 0.81618255

00:39:54.230 --> 00:39:57.319 example this particular PDE gets metabolised,

NOTE Confidence: 0.81618255

 $00:39:57.320 \longrightarrow 00:40:00.860$  it gets this hydroxyl group added.

NOTE Confidence: 0.81618255

 $00:40:00.860 \longrightarrow 00:40:03.884$  And now even more closely resembles

NOTE Confidence: 0.81618255

 $00:40:03.884 \longrightarrow 00:40:07.923$  Thyrax in so the in vitro studies

NOTE Confidence: 0.81618255

 $00:40:07.923 \longrightarrow 00:40:11.763$  have shown that these chemicals can

NOTE Confidence: 0.81618255

 $00:40:11.763 \longrightarrow 00:40:14.598$  competitively binds with thyroid

NOTE Confidence: 0.81618255

 $00{:}40{:}14.598 \operatorname{--}{>} 00{:}40{:}18.088$  transport proteins and results in

NOTE Confidence: 0.81618255

 $00:40:18.088 \longrightarrow 00:40:21.242$  reduced circulation of thyroid hormones,

NOTE Confidence: 0.81618255

 $00{:}40{:}21.242 \dashrightarrow 00{:}40{:}24.746$  which could then result in dysregulation

NOTE Confidence: 0.81618255

00:40:24.746 --> 00:40:28.809 of the transport and signaling pathways,

NOTE Confidence: 0.81618255

 $00:40:28.810 \longrightarrow 00:40:30.832$  potentially leading to.

NOTE Confidence: 0.81618255

00:40:30.832 --> 00:40:31.506 Overproduction,

NOTE Confidence: 0.81618255

 $00:40:31.506 \longrightarrow 00:40:34.876$  of of hormones to compensate

 $00:40:34.876 \longrightarrow 00:40:37.323$  proliferation in the thyroid

NOTE Confidence: 0.81618255

 $00{:}40{:}37.323 \dashrightarrow 00{:}40{:}39.009$  and potentially neoplasia.

NOTE Confidence: 0.85149497

 $00:40:41.810 \longrightarrow 00:40:45.198$  So as you know the the hypothalamus,

NOTE Confidence: 0.85149497

00:40:45.200 --> 00:40:47.615 pituitary, thyroid axis is this

NOTE Confidence: 0.85149497

 $00:40:47.615 \longrightarrow 00:40:49.547$  very well choreographed system.

NOTE Confidence: 0.85149497

 $00:40:49.550 \longrightarrow 00:40:51.574$  So these perturbations or

NOTE Confidence: 0.85149497

 $00:40:51.574 \longrightarrow 00:40:53.598$  dysregulation of these systems

NOTE Confidence: 0.85149497

 $00:40:53.598 \longrightarrow 00:40:56.327$  can perhaps trigger some of these.

NOTE Confidence: 0.85149497

 $00:40:56.330 \longrightarrow 00:40:59.168$  Some proliferation of the thyroid and

NOTE Confidence: 0.85149497

00:40:59.168 --> 00:41:01.650 potentially lead to thyroid cancer.

NOTE Confidence: 0.85149497

00:41:01.650 --> 00:41:03.990 I'm just I'm showing this slide

NOTE Confidence: 0.85149497

 $00:41:03.990 \longrightarrow 00:41:06.231$  to also illustrate that some

NOTE Confidence: 0.85149497

 $00{:}41{:}06.231 \dashrightarrow 00{:}41{:}08.663$  chemicals have some additional

NOTE Confidence: 0.85149497

 $00:41:08.663 \longrightarrow 00:41:10.912$  hypothesized mechanisms, such as.

NOTE Confidence: 0.85149497

 $00:41:10.912 \longrightarrow 00:41:14.008$  Some have been shown to be

NOTE Confidence: 0.85149497

 $00:41:14.008 \longrightarrow 00:41:17.510$  capable to directly bind to DNA,

00:41:17.510 --> 00:41:20.606 leading to mutations and could potentially

NOTE Confidence: 0.85149497

 $00:41:20.606 \longrightarrow 00:41:23.040$  lead to carcinogenesis that way.

NOTE Confidence: 0.83227754

00:41:26.390 --> 00:41:28.976 So before we launched our study,

NOTE Confidence: 0.83227754

 $00:41:28.980 \longrightarrow 00:41:31.572$  there had only been two other

NOTE Confidence: 0.83227754

 $00:41:31.572 \longrightarrow 00:41:33.300$  studies examining this hypothesis.

NOTE Confidence: 0.83227754

 $00:41:33.300 \longrightarrow 00:41:35.766$  This idea that these PPDS could

NOTE Confidence: 0.83227754

 $00:41:35.766 \longrightarrow 00:41:38.050$  be linked to thyroid cancer.

NOTE Confidence: 0.83227754

 $00:41:38.050 \longrightarrow 00:41:41.902$  So the first two rows of this table or

NOTE Confidence: 0.83227754

 $00{:}41{:}41.902 \dashrightarrow 00{:}41{:}45.292$  the two prior epidemiologic studies in

NOTE Confidence: 0.83227754

 $00{:}41{:}45.292 \dashrightarrow 00{:}41{:}50.089$  the third row was the study that I lead.

NOTE Confidence: 0.83227754

 $00:41:50.090 \longrightarrow 00:41:53.202$  A couple things to point out here is

NOTE Confidence: 0.83227754

 $00:41:53.202 \longrightarrow 00:41:56.763$  that the case is the studies that came

NOTE Confidence: 0.83227754

 $00{:}41{:}56.763 \dashrightarrow 00{:}42{:}00.209$  before us had moderate study populations,

NOTE Confidence: 0.83227754

 $00:42:00.210 \longrightarrow 00:42:01.878$  and ours was larger.

NOTE Confidence: 0.83227754

 $00:42:01.878 \longrightarrow 00:42:03.963$  We also looked at more

 $00:42:03.963 \longrightarrow 00:42:05.730$  chemicals and importantly,

NOTE Confidence: 0.83227754

 $00:42:05.730 \longrightarrow 00:42:08.030$  we looked at single and

NOTE Confidence: 0.83227754

 $00:42:08.030 \longrightarrow 00:42:09.870$  multi pollutant models so.

NOTE Confidence: 0.8642995

 $00:42:12.080 \longrightarrow 00:42:14.798$  So what I mean by that is that in

NOTE Confidence: 0.8642995

00:42:14.798 --> 00:42:17.775 the real world you know we're not

NOTE Confidence: 0.8642995

00:42:17.775 --> 00:42:20.409 exposed to one chemical at a time,

NOTE Confidence: 0.8642995

 $00:42:20.410 \longrightarrow 00:42:22.222$  where typically exposed to groups of

NOTE Confidence: 0.8642995

00:42:22.222 --> 00:42:23.982 chemicals or mixtures of chemicals

NOTE Confidence: 0.8642995

 $00:42:23.982 \longrightarrow 00:42:25.470$  and traditional environmental.

NOTE Confidence: 0.8642995

00:42:25.470 --> 00:42:26.918 Epidemiologic studies have looked

NOTE Confidence: 0.8642995

 $00:42:26.918 \longrightarrow 00:42:29.460$  at chemicals just one at a time,

NOTE Confidence: 0.8642995

00:42:29.460 --> 00:42:31.728 and in my work we're looking at

NOTE Confidence: 0.8642995

 $00:42:31.728 \longrightarrow 00:42:33.132$  these so-called mixtures using

NOTE Confidence: 0.8642995

 $00{:}42{:}33.132 \dashrightarrow 00{:}42{:}34.227$  different modeling techniques

NOTE Confidence: 0.8642995

 $00:42:34.227 \longrightarrow 00:42:36.886$  to look at the joint effect of

NOTE Confidence: 0.8642995

 $00:42:36.886 \longrightarrow 00:42:38.510$  exposures to multiple chemicals.

00:42:41.910 --> 00:42:43.554 Similarly for the PCB's,

NOTE Confidence: 0.8465663

 $00:42:43.554 \longrightarrow 00:42:46.479$  the other chemicals there were also only

NOTE Confidence: 0.8465663

 $00:42:46.479 \longrightarrow 00:42:49.174$  two previous studies before we did ours.

NOTE Confidence: 0.8465663

 $00:42:49.180 \longrightarrow 00:42:52.052$  Also the other studies were a bit smaller

NOTE Confidence: 0.8465663

 $00:42:52.052 \longrightarrow 00:42:55.236$  and we also looked at mixture modeling.

NOTE Confidence: 0.8465663

 $00:42:55.240 \longrightarrow 00:42:57.008$  One other one shortcoming,

NOTE Confidence: 0.8465663

00:42:57.008 --> 00:43:00.502 I wanted to point out actually in reference

NOTE Confidence: 0.8465663

 $00:43:00.502 \longrightarrow 00:43:03.993$  to at least one of the other studies is

NOTE Confidence: 0.8465663

 $00{:}43{:}03.993 \dashrightarrow 00{:}43{:}06.953$  that our study was a case control study.

NOTE Confidence: 0.8465663

 $00:43:06.960 \longrightarrow 00:43:11.217$  So we did collect serum samples to do our.

NOTE Confidence: 0.8465663

00:43:11.220 --> 00:43:12.204 Environmental chemical

NOTE Confidence: 0.8465663

 $00:43:12.204 \longrightarrow 00:43:13.680$  measurements after diagnosis.

NOTE Confidence: 0.8465663

 $00:43:13.680 \longrightarrow 00:43:15.648$  Whereas one other study

NOTE Confidence: 0.8465663

00:43:15.648 --> 00:43:17.616 collected pre diagnosis samples,

NOTE Confidence: 0.8465663

 $00:43:17.620 \longrightarrow 00:43:19.580$  we think you know.

00:43:19.580 --> 00:43:23.096 So we're using this post diagnosis sample

NOTE Confidence: 0.8465663

 $00{:}43{:}23.096 \dashrightarrow 00{:}43{:}26.952$  to try to capture exposures in the past.

NOTE Confidence: 0.8465663

00:43:26.960 --> 00:43:28.596 While it's not optimal,

NOTE Confidence: 0.8465663

 $00:43:28.596 \longrightarrow 00:43:31.772$  we think this is actually a pretty

NOTE Confidence: 0.8465663

 $00:43:31.772 \longrightarrow 00:43:34.336$  strong and reasonable assumption,

NOTE Confidence: 0.8465663

 $00{:}43{:}34.340 \dashrightarrow 00{:}43{:}37.586$  because we know that these chemicals

NOTE Confidence: 0.8465663

 $00{:}43{:}37.586 \dashrightarrow 00{:}43{:}41.630$  have half lives of years and decades.

NOTE Confidence: 0.8465663

 $00:43:41.630 \longrightarrow 00:43:44.540$  Ends may may well reflect past

NOTE Confidence: 0.8465663

 $00{:}43{:}44.540 \dashrightarrow 00{:}43{:}47.470$  past you some past exposure.

NOTE Confidence: 0.8271222

 $00:43:50.580 \longrightarrow 00:43:53.191$  OK, so just a few more details

NOTE Confidence: 0.8271222

 $00:43:53.191 \longrightarrow 00:43:55.449$  about the study we conducted.

NOTE Confidence: 0.8271222

 $00{:}43{:}55.450 \dashrightarrow 00{:}43{:}58.034$  I LED a study within a study and

NOTE Confidence: 0.8271222

 $00:43:58.034 \longrightarrow 00:44:00.719$  that larger study was the Connecticut

NOTE Confidence: 0.8271222

00:44:00.719 --> 00:44:03.169 thyroid cancer case control study,

NOTE Confidence: 0.8271222

00:44:03.170 --> 00:44:05.600 which was led by Yahweh Chung,

NOTE Confidence: 0.8271222

 $00{:}44{:}05.600 \dashrightarrow 00{:}44{:}07.535$  who was our former colleague

 $00:44:07.535 \longrightarrow 00:44:10.070$  here at the Yale Cancer Center.

NOTE Confidence: 0.8271222

 $00:44:10.070 \longrightarrow 00:44:12.422$  We focused on women because they

NOTE Confidence: 0.8271222

 $00:44:12.422 \longrightarrow 00:44:14.940$  have that three times higher risk.

NOTE Confidence: 0.8271222

 $00:44:14.940 \longrightarrow 00:44:17.376$  I showed earlier about 90% of

NOTE Confidence: 0.8271222

 $00:44:17.376 \longrightarrow 00:44:19.986$  our cases were white, so we.

NOTE Confidence: 0.8271222

00:44:19.986 --> 00:44:22.451 Focused on the white population

NOTE Confidence: 0.8271222

00:44:22.451 --> 00:44:25.682 because our numbers were really small

NOTE Confidence: 0.8271222

 $00:44:25.682 \longrightarrow 00:44:28.447$  for looking at other demographics.

NOTE Confidence: 0.8271222

00:44:28.450 --> 00:44:31.824 I do think now this is something

NOTE Confidence: 0.8271222

 $00:44:31.824 \longrightarrow 00:44:35.685$  I would like to follow up on

NOTE Confidence: 0.8271222

00:44:35.685 --> 00:44:37.989 more in another population,

NOTE Confidence: 0.8271222

 $00:44:37.990 \longrightarrow 00:44:41.170$  we focused on papillary thyroid cancers.

NOTE Confidence: 0.8271222

 $00:44:41.170 \longrightarrow 00:44:43.820$  That's about 85% of the

NOTE Confidence: 0.8271222

 $00:44:43.820 \longrightarrow 00:44:45.940$  new cases or papillary.

NOTE Confidence: 0.8271222

 $00:44:45.940 \longrightarrow 00:44:48.590$  We also collected very detailed

00:44:48.590 --> 00:44:50.180 information about demographics,

NOTE Confidence: 0.8271222

00:44:50.180 --> 00:44:51.158 lifestyle, diet.

NOTE Confidence: 0.8271222

 $00:44:51.158 \longrightarrow 00:44:54.092$  Many other risk factors that we

NOTE Confidence: 0.8271222

 $00:44:54.092 \longrightarrow 00:44:56.620$  can control for other factors.

NOTE Confidence: 0.8271222

 $00:44:56.620 \longrightarrow 00:44:58.960$  We collected the blood sample at

NOTE Confidence: 0.8271222

 $00:44:58.960 \longrightarrow 00:45:02.190$  the time of the interview and then

NOTE Confidence: 0.8271222

 $00:45:02.190 \longrightarrow 00:45:04.830$  measured the participants blood samples

NOTE Confidence: 0.8271222

00:45:04.830 --> 00:45:08.087 for 11 different peyizan 32 PCBS,

NOTE Confidence: 0.8271222

 $00{:}45{:}08.090 \dashrightarrow 00{:}45{:}10.958$  which this analysis also gave us.

NOTE Confidence: 0.8271222

00:45:10.960 --> 00:45:12.856 Some pesticides like DDT,

NOTE Confidence: 0.8271222

 $00:45:12.856 \longrightarrow 00:45:16.220$  which are also structurally similar to these.

NOTE Confidence: 0.8271222

 $00:45:16.220 \longrightarrow 00:45:19.388$  These classes of chemicals.

NOTE Confidence: 0.8271222

00:45:19.390 --> 00:45:22.127 And again we looked at both pollutants,

NOTE Confidence: 0.8271222

 $00:45:22.130 \longrightarrow 00:45:25.586$  one at a time, like like most studies

NOTE Confidence: 0.8271222

 $00:45:25.586 \longrightarrow 00:45:29.308$  do and then multi pollutant models.

NOTE Confidence: 0.8271222

 $00:45:29.310 \longrightarrow 00:45:31.872$  OK, so here's some results from

00:45:31.872 --> 00:45:33.153 our study population.

NOTE Confidence: 0.8271222

 $00:45:33.160 \longrightarrow 00:45:35.295$  These are factors that differed

NOTE Confidence: 0.8271222

 $00:45:35.295 \longrightarrow 00:45:37.003$  between cases and controls,

NOTE Confidence: 0.8271222

00:45:37.010 --> 00:45:39.824 so our cases had a lower educational

NOTE Confidence: 0.8271222

 $00:45:39.824 \longrightarrow 00:45:41.720$  attainment compared to controls.

NOTE Confidence: 0.8271222

 $00:45:41.720 \longrightarrow 00:45:43.855$  They did have a history

NOTE Confidence: 0.8271222

 $00:45:43.855 \longrightarrow 00:45:45.563$  of benign thyroid disease.

NOTE Confidence: 0.8271222

 $00:45:45.570 \longrightarrow 00:45:48.002$  That's a strong risk

NOTE Confidence: 0.8271222

 $00:45:48.002 \longrightarrow 00:45:50.434$  factor for thyroid cancer.

NOTE Confidence: 0.8271222

 $00:45:50.440 \longrightarrow 00:45:54.628$  Alcohol consumption was actually.

NOTE Confidence: 0.8271222

 $00{:}45{:}54.630 --> 00{:}45{:}55.582 \ \mathrm{Higher,\ lower,}$ 

NOTE Confidence: 0.8271222

 $00:45:55.582 \longrightarrow 00:45:57.010$  lower in cases.

NOTE Confidence: 0.8271222

00:45:57.010 --> 00:46:00.482 This is one of the few cancers where

NOTE Confidence: 0.8271222

 $00:46:00.482 \longrightarrow 00:46:02.968$  alcohol actually has been consistently

NOTE Confidence: 0.8271222

 $00:46:02.968 \longrightarrow 00:46:06.028$  shown to have a protective effect.

 $00:46:06.030 \longrightarrow 00:46:09.229$  An cases also had a history of

NOTE Confidence: 0.8271222

00:46:09.229 --> 00:46:11.730 thyroid cancer and higher BMI,

NOTE Confidence: 0.8271222

 $00:46:11.730 \longrightarrow 00:46:14.936$  which has been shown now in several

NOTE Confidence: 0.8271222

 $00:46:14.936 \longrightarrow 00:46:16.817$  studies indicating another possible

NOTE Confidence: 0.8271222

00:46:16.817 --> 00:46:19.385 risk risk factor that can also

NOTE Confidence: 0.8271222

00:46:19.385 --> 00:46:21.860 be interrelated to like endocrine

NOTE Confidence: 0.8271222

 $00:46:21.860 \longrightarrow 00:46:24.076$  disrupting chemicals and also.

NOTE Confidence: 0.8689489

 $00:46:26.490 \longrightarrow 00:46:29.479$  OK, so here are some results from

NOTE Confidence: 0.8689489

 $00{:}46{:}29.479 \to 00{:}46{:}32.012$  our single pollutant models where we

NOTE Confidence: 0.8689489

 $00:46:32.012 \longrightarrow 00:46:34.728$  looked at one chemical at a time.

NOTE Confidence: 0.8689489

 $00{:}46{:}34.730 \dashrightarrow 00{:}46{:}36.995$  So these are increasing categories

NOTE Confidence: 0.8689489

 $00:46:36.995 \longrightarrow 00:46:39.260$  of exposure within each of

NOTE Confidence: 0.8689489

 $00:46:39.342 \longrightarrow 00:46:41.349$  these different pollutants.

NOTE Confidence: 0.8689489

00:46:41.350 --> 00:46:44.806 You know, odds Ratio 1 means no effects,

NOTE Confidence: 0.8689489

 $00:46:44.810 \longrightarrow 00:46:48.104$  and anything above one would indicate

NOTE Confidence: 0.8689489

 $00:46:48.104 \longrightarrow 00:46:50.980$  an Association with thyroid cancer.

 $00:46:50.980 \longrightarrow 00:46:53.654$  So you can see here that there's

NOTE Confidence: 0.8689489

 $00{:}46{:}53.654 \dashrightarrow 00{:}46{:}56.395$  really not much going on with

NOTE Confidence: 0.8689489

 $00:46:56.395 \longrightarrow 00:46:57.907$  these individual models.

NOTE Confidence: 0.8689489

00:46:57.910 --> 00:47:00.268 If anything, the odds of thyroid

NOTE Confidence: 0.8689489

 $00{:}47{:}00.268 \longrightarrow 00{:}47{:}03.292$  cancer seem to be lower than those

NOTE Confidence: 0.8689489

 $00:47:03.292 \longrightarrow 00:47:06.028$  who are exposed compared to the

NOTE Confidence: 0.8689489

00:47:06.028 --> 00:47:08.300 reference group of low exposure.

NOTE Confidence: 0.8689489

 $00:47:08.300 \longrightarrow 00:47:10.778$  So the medium and high groups are

NOTE Confidence: 0.8689489

 $00:47:10.778 \longrightarrow 00:47:13.941$  not at an elevated odds of thyroid

NOTE Confidence: 0.8689489

 $00:47:13.941 \longrightarrow 00:47:16.959$  cancer except for this one chemical.

NOTE Confidence: 0.8689489

 $00{:}47{:}16.960 \dashrightarrow 00{:}47{:}18.259$  This PB 153.

NOTE Confidence: 0.79854375

 $00:47:21.870 \longrightarrow 00:47:24.648$  So when we move to our

NOTE Confidence: 0.79854375

00:47:24.648 --> 00:47:26.037 multi pollutant models,

NOTE Confidence: 0.79854375

 $00:47:26.040 \longrightarrow 00:47:28.818$  the results are also somewhat null.

NOTE Confidence: 0.79854375

 $00:47:28.820 \longrightarrow 00:47:31.598$  We have two multi pollutant models

00:47:31.598 --> 00:47:33.450 here using Bayesian modeling,

NOTE Confidence: 0.79854375

 $00:47:33.450 \longrightarrow 00:47:36.216$  which I won't get into here.

NOTE Confidence: 0.79854375

 $00:47:36.220 \longrightarrow 00:47:39.556$  But here you can see that it's the

NOTE Confidence: 0.79854375

 $00:47:39.556 \longrightarrow 00:47:43.168$  picture is still pretty null except for.

NOTE Confidence: 0.79854375

 $00:47:43.170 \longrightarrow 00:47:46.404$  In this case we have this other,

NOTE Confidence: 0.79854375

 $00:47:46.410 \longrightarrow 00:47:49.030$  a different chemical PDE 100.

NOTE Confidence: 0.79854375

 $00:47:49.030 \longrightarrow 00:47:52.306$  Was associated with elevated odds of

NOTE Confidence: 0.79854375

 $00:47:52.306 \longrightarrow 00:47:55.730$  thyroid cancer using both those models.

NOTE Confidence: 0.8645845

 $00{:}47{:}57.760 \dashrightarrow 00{:}48{:}00.888$  And then finally we did this one more

NOTE Confidence: 0.8645845

00:48:00.888 --> 00:48:03.478 mixture type approach of principle,

NOTE Confidence: 0.8645845

 $00:48:03.480 \longrightarrow 00:48:06.978$  components analysis and in this work

NOTE Confidence: 0.8645845

 $00:48:06.978 \longrightarrow 00:48:11.159$  we found that people who had had this.

NOTE Confidence: 0.8645845

 $00:48:11.160 \longrightarrow 00:48:14.796$  Combination of exposures which was higher.

NOTE Confidence: 0.8645845

 $00:48:14.800 \longrightarrow 00:48:19.280$  PBDE 153. An lower PDE 209 had an

NOTE Confidence: 0.8645845

 $00:48:19.280 \longrightarrow 00:48:22.669$  elevated odds of thyroid cancer.

NOTE Confidence: 0.8226875

 $00:48:26.300 \longrightarrow 00:48:29.850$  So then moving on to the PCB use in this

 $00:48:29.942 \longrightarrow 00:48:33.134$  for this one because we had so many,

NOTE Confidence: 0.8226875

 $00:48:33.140 \longrightarrow 00:48:35.040$  we had 32 different chemicals.

NOTE Confidence: 0.8226875

00:48:35.040 --> 00:48:37.574 I'm just going to present some some

NOTE Confidence: 0.8226875

00:48:37.574 --> 00:48:39.599 groups of structurally similar PCB's,

NOTE Confidence: 0.8226875

 $00:48:39.600 \longrightarrow 00:48:41.754$  which was another approach we used

NOTE Confidence: 0.8226875

 $00:48:41.754 \longrightarrow 00:48:44.160$  to look at groups of chemicals.

NOTE Confidence: 0.8226875

00:48:44.160 --> 00:48:48.120 So in this in this model this kind of

NOTE Confidence: 0.8226875

 $00:48:48.120 \longrightarrow 00:48:52.358$  we're just looking at one group at a time.

NOTE Confidence: 0.8226875

00:48:52.360 --> 00:48:55.096 Odds ratios are hovering around 1:00,

NOTE Confidence: 0.8226875

 $00:48:55.100 \longrightarrow 00:48:57.966$  so again pretty null findings. Not.

NOTE Confidence: 0.8226875

 $00{:}48{:}57.966 {\:{\mbox{--}}}{>} 00{:}49{:}01.422$  We're not seeing a link between

NOTE Confidence: 0.8226875

 $00:49:01.422 \longrightarrow 00:49:03.960$  exposure and thyroid cancer.

NOTE Confidence: 0.8226875

 $00{:}49{:}03.960 \dashrightarrow 00{:}49{:}08.056$  However, it said the most intriguing part of

NOTE Confidence: 0.8226875

 $00:49:08.056 \longrightarrow 00:49:12.348$  this study was when we took a closer look at.

NOTE Confidence: 0.8226875

 $00:49:12.350 \longrightarrow 00:49:14.320$  The the groups of people,

 $00:49:14.320 \longrightarrow 00:49:17.468$  people who are exposed.

NOTE Confidence: 0.8226875

 $00:49:17.470 \longrightarrow 00:49:19.650$  During who were younger

NOTE Confidence: 0.8226875

00:49:19.650 --> 00:49:21.285 during peak production,

NOTE Confidence: 0.8226875

 $00:49:21.290 \longrightarrow 00:49:24.015$  who were born during peak

NOTE Confidence: 0.8226875

 $00:49:24.015 \longrightarrow 00:49:25.650$  production of PCB's.

NOTE Confidence: 0.8226875

 $00:49:25.650 \longrightarrow 00:49:28.375$  So presumably would have their

NOTE Confidence: 0.8226875

 $00:49:28.375 \longrightarrow 00:49:31.640$  highest exposure in very early life.

NOTE Confidence: 0.8226875

 $00:49:31.640 \longrightarrow 00:49:33.820$  They consistently had higher

NOTE Confidence: 0.8226875

 $00:49:33.820 \longrightarrow 00:49:36.000$  odds of thyroid cancer,

NOTE Confidence: 0.8226875

 $00:49:36.000 \longrightarrow 00:49:39.300$  including this group of PCB's that

NOTE Confidence: 0.8226875

 $00{:}49{:}39.300 \dashrightarrow 00{:}49{:}40.950$  were particularly structurally

NOTE Confidence: 0.8226875

 $00:49:40.950 \longrightarrow 00:49:43.090$  similar to thyroid hormones,

NOTE Confidence: 0.8226875

 $00:49:43.090 \longrightarrow 00:49:46.898$  so this was quite intriguing to me,

NOTE Confidence: 0.8226875

 $00:49:46.900 \longrightarrow 00:49:49.152$  suggesting maybe the timing.

NOTE Confidence: 0.8226875

 $00:49:49.152 \longrightarrow 00:49:51.967$  Of exposure could be important.

NOTE Confidence: 0.8235304

 $00:49:54.220 \longrightarrow 00:49:57.994$  OK. So just to summarize,

 $00:49:57.994 \longrightarrow 00:50:00.400$  some of the key takeaways from both.

NOTE Confidence: 0.8235304

 $00:50:00.400 \longrightarrow 00:50:03.430$  Of these studies.

NOTE Confidence: 0.8235304

 $00{:}50{:}03.430 \dashrightarrow 00{:}50{:}05.929$  Strengths were that we looked at this

NOTE Confidence: 0.8235304

 $00:50:05.929 \longrightarrow 00:50:07.456$  larger population and incorporated

NOTE Confidence: 0.8235304

 $00:50:07.456 \longrightarrow 00:50:09.814$  these different models to account for

NOTE Confidence: 0.8235304

 $00:50:09.814 \longrightarrow 00:50:12.269$  Co exposure to multiple pollutants.

NOTE Confidence: 0.8235304

 $00:50:12.270 \longrightarrow 00:50:14.280$  The results were generally null.

NOTE Confidence: 0.8235304

 $00:50:14.280 \longrightarrow 00:50:16.880$  You know, we did see a few chemicals

NOTE Confidence: 0.8235304

 $00:50:16.880 \longrightarrow 00:50:19.074$  here and their associated with

NOTE Confidence: 0.8235304

 $00:50:19.074 \longrightarrow 00:50:21.514$  elevated odds of thyroid cancer.

NOTE Confidence: 0.8235304

00:50:21.520 --> 00:50:21.938 Particularly,

NOTE Confidence: 0.8235304

 $00:50:21.938 \longrightarrow 00:50:24.446$  this was more consistent when we

NOTE Confidence: 0.8235304

 $00{:}50{:}24.446 \dashrightarrow 00{:}50{:}27.655$  looked at the group of women who were

NOTE Confidence: 0.8235304

 $00:50:27.655 \longrightarrow 00:50:29.960$  born during peak production of PCBS.

NOTE Confidence: 0.8235304

00:50:29.960 --> 00:50:33.176 However, this we only have 3 studies now.

 $00:50:33.180 \longrightarrow 00:50:34.028$  For these,

NOTE Confidence: 0.8235304

 $00{:}50{:}34.028 \dashrightarrow 00{:}50{:}36.996$  each of these groups of chemicals so.

NOTE Confidence: 0.8235304

 $00:50:37.000 \longrightarrow 00:50:38.089$  There's really insufficient

NOTE Confidence: 0.8235304

 $00:50:38.089 \longrightarrow 00:50:39.904$  evidence to rule them out,

NOTE Confidence: 0.8235304

 $00:50:39.910 \longrightarrow 00:50:42.381$  and I think there can be some

NOTE Confidence: 0.8235304

00:50:42.381 --> 00:50:44.615 improvements to the study design to

NOTE Confidence: 0.8235304

 $00:50:44.615 \longrightarrow 00:50:47.184$  try to look at this more carefully.

NOTE Confidence: 0.8235304

 $00:50:47.190 \longrightarrow 00:50:49.010$  I think looking at early

NOTE Confidence: 0.8235304

00:50:49.010 --> 00:50:50.466 life would be important,

NOTE Confidence: 0.8235304

 $00:50:50.470 \longrightarrow 00:50:52.558$  and using a prospective design where

NOTE Confidence: 0.8235304

 $00:50:52.558 \longrightarrow 00:50:54.393$  we could have samples collected

NOTE Confidence: 0.8235304

 $00:50:54.393 \longrightarrow 00:50:56.655$  pre diagnosis could help you know.

NOTE Confidence: 0.8235304

 $00:50:56.660 \longrightarrow 00:50:57.135$  Really,

NOTE Confidence: 0.8235304

00:50:57.135 --> 00:50:59.985 try to nail nail down if

NOTE Confidence: 0.8235304

 $00:50:59.985 \longrightarrow 00:51:02.269$  anything is going on here.

NOTE Confidence: 0.8235304

 $00:51:02.270 \longrightarrow 00:51:05.422$  And then finally I just want to talk

 $00:51:05.422 \longrightarrow 00:51:08.618$  about how where I'm taking this work.

NOTE Confidence: 0.8235304

 $00:51:08.620 \longrightarrow 00:51:11.434$  I have now expanded this work in

NOTE Confidence: 0.8235304

 $00:51:11.434 \longrightarrow 00:51:13.690$  adults to looking at children.

NOTE Confidence: 0.8235304

00:51:13.690 --> 00:51:16.228 So with my collaborator Xiaomei MA,

NOTE Confidence: 0.8235304

 $00:51:16.230 \longrightarrow 00:51:19.184$  also very active in the Cancer Center.

NOTE Confidence: 0.8235304

00:51:19.190 --> 00:51:21.305 We are looking at environmental

NOTE Confidence: 0.8235304

00:51:21.305 --> 00:51:23.420 exposures and pediatric thyroid cancer,

NOTE Confidence: 0.8235304

 $00:51:23.420 \longrightarrow 00:51:25.112$  so here's some incidents.

NOTE Confidence: 0.8235304

 $00{:}51{:}25.112 \dashrightarrow 00{:}51{:}27.227$  Data on pediatric thyroid cancer.

NOTE Confidence: 0.8235304

 $00:51:27.230 \longrightarrow 00:51:30.184$  It has also been increasing over time.

NOTE Confidence: 0.8235304

 $00:51:30.190 \longrightarrow 00:51:32.360$  An children are less likely.

NOTE Confidence: 0.8235304

 $00:51:32.360 \longrightarrow 00:51:35.330$  To be.

NOTE Confidence: 0.8235304

 $00:51:35.330 \longrightarrow 00:51:37.070$  Targeted for increased screening

NOTE Confidence: 0.8235304

 $00:51:37.070 \longrightarrow 00:51:38.810$  and diagnosis and imaging,

NOTE Confidence: 0.8235304

 $00:51:38.810 \longrightarrow 00:51:41.420$  so these trends are are concerning,

00:51:41.420 --> 00:51:43.786 so we have some projects underway to

NOTE Confidence: 0.8235304

 $00:51:43.786 \longrightarrow 00:51:46.514$  try to look at environmental exposures

NOTE Confidence: 0.8235304

 $00:51:46.514 \longrightarrow 00:51:49.244$  in this more vulnerable population.

NOTE Confidence: 0.8235304

 $00:51:49.250 \longrightarrow 00:51:51.784$  And with that I would like to

NOTE Confidence: 0.8235304

 $00:51:51.784 \longrightarrow 00:51:53.474$  acknowledge all my wonderful

NOTE Confidence: 0.8235304

00:51:53.474 --> 00:51:56.114 collaborators and my funding from

NOTE Confidence: 0.8235304

 $00{:}51{:}56.114 \dashrightarrow 00{:}51{:}59.100$  American Cancer Society as well as

NOTE Confidence: 0.8235304

00:51:59.100 --> 00:52:01.494 the Yale Cancer Center for getting

NOTE Confidence: 0.8235304

 $00{:}52{:}01.494 \dashrightarrow 00{:}52{:}04.480$  me started in this line of research.

NOTE Confidence: 0.8235304

 $00:52:04.480 \longrightarrow 00:52:05.350$  Thank you.

NOTE Confidence: 0.89094794

 $00:52:06.930 \longrightarrow 00:52:08.298$  Thank you Doctor Diesel,

NOTE Confidence: 0.89094794

 $00:52:08.298 \longrightarrow 00:52:09.324$  that was fantastic.

NOTE Confidence: 0.89094794

 $00:52:09.330 \longrightarrow 00:52:10.320$  A little alarming.

NOTE Confidence: 0.89094794

 $00:52:10.320 \longrightarrow 00:52:12.630$  I would say when we start to

NOTE Confidence: 0.89094794

00:52:12.708 --> 00:52:14.820 think about how many you know,

NOTE Confidence: 0.89094794

 $00{:}52{:}14.820 \dashrightarrow 00{:}52{:}16.535$  carcinogens exist in our environment

00:52:16.535 --> 00:52:18.960 in the fact that I'm intrigued by

NOTE Confidence: 0.89094794

 $00{:}52{:}18.960 \to 00{:}52{:}21.235$  the policy statement that we have to

NOTE Confidence: 0.89094794

 $00:52:21.235 \longrightarrow 00:52:23.714$  show harm before anything can be done

NOTE Confidence: 0.89094794

 $00:52:23.714 \longrightarrow 00:52:25.453$  and have these substances banned.

NOTE Confidence: 0.89094794

 $00:52:25.453 \longrightarrow 00:52:27.511$  Do you think there's any potential

NOTE Confidence: 0.89094794

 $00:52:27.511 \longrightarrow 00:52:29.274$  to being able to reverse

NOTE Confidence: 0.89094794

 $00:52:29.274 \longrightarrow 00:52:30.939$  that or change that policy?

NOTE Confidence: 0.89094794

00:52:30.940 --> 00:52:34.710 Or will it take years and more data to do so?

NOTE Confidence: 0.86721903

 $00:52:35.300 \longrightarrow 00:52:37.910$  Yeah, so a lot of the chemicals were kind

NOTE Confidence: 0.86721903

 $00:52:37.910 \longrightarrow 00:52:41.241$  of grandfathered in when we established the

NOTE Confidence: 0.86721903

 $00:52:41.241 \longrightarrow 00:52:43.620$  Environmental Protection Agency in 1970.

NOTE Confidence: 0.86721903

 $00{:}52{:}43.620 \dashrightarrow 00{:}52{:}46.612$  There is a new act that is supposed

NOTE Confidence: 0.86721903

00:52:46.612 --> 00:52:49.157 to reverse this burden of proof,

NOTE Confidence: 0.86721903

00:52:49.160 --> 00:52:52.320 but I don't think it's going to be

NOTE Confidence: 0.86721903

 $00:52:52.320 \longrightarrow 00:52:55.192$  retroactive, so I am encouraged to with

 $00:52:55.192 \longrightarrow 00:52:57.653$  the current administration that we may

NOTE Confidence: 0.86721903

 $00:52:57.653 \longrightarrow 00:53:00.250$  start to move towards a different model.

NOTE Confidence: 0.86721903

00:53:00.250 --> 00:53:02.896 Also, in Europe they have stronger

NOTE Confidence: 0.86721903

 $00:53:02.896 \longrightarrow 00:53:05.077$  precautionary policies where if there's

NOTE Confidence: 0.86721903

 $00:53:05.077 \longrightarrow 00:53:07.869$  a safer alternative you have to use it.

NOTE Confidence: 0.86721903

00:53:07.870 --> 00:53:11.214 And you know not to wait until we

NOTE Confidence: 0.86721903

 $00:53:11.214 \longrightarrow 00:53:13.513$  prove something with certainty to

NOTE Confidence: 0.86721903

 $00:53:13.513 \longrightarrow 00:53:15.803$  take some sort of action.

NOTE Confidence: 0.7947095

 $00{:}53{:}15.810 \longrightarrow 00{:}53{:}19.258$  Great, right? So there's a couple of chat

NOTE Confidence: 0.7947095

00:53:19.258 --> 00:53:21.978 questions I'll just quickly read them.

NOTE Confidence: 0.7947095

 $00{:}53{:}21.980 \dashrightarrow 00{:}53{:}25.508$  Heard a Chow asked about any data on

NOTE Confidence: 0.7947095

00:53:25.510 --> 00:53:27.720 Agent Orange and thyroid cancer.

NOTE Confidence: 0.7947095

 $00:53:27.720 \longrightarrow 00:53:30.667$  Yeah, so Dioxin's is one of the

NOTE Confidence: 0.7947095

00:53:30.667 --> 00:53:32.570 constituents of Agent Orange.

NOTE Confidence: 0.7947095

00:53:32.570 --> 00:53:33.893 Well, Agent Orange.

NOTE Confidence: 0.7947095

 $00:53:33.893 \longrightarrow 00:53:36.539$  Had you know these defoliant chemicals?

 $00:53:36.540 \longrightarrow 00:53:37.902$  So various herbicides?

NOTE Confidence: 0.7947095

 $00:53:37.902 \longrightarrow 00:53:39.900$  And then? Dioxin's

NOTE Confidence: 0.81728315

 $00:53:42.160 \longrightarrow 00:53:43.660$  that's a great question,

NOTE Confidence: 0.81728315

 $00:53:43.660 \longrightarrow 00:53:45.535$  'cause they're also very structurally

NOTE Confidence: 0.81728315

 $00:53:45.535 \longrightarrow 00:53:47.213$  similar to the other chemicals

NOTE Confidence: 0.81728315

00:53:47.213 --> 00:53:49.208 I presented, but I'd have to,

NOTE Confidence: 0.81728315

00:53:49.208 --> 00:53:52.099 and some of the chemicals we looked at.

NOTE Confidence: 0.81728315

00:53:52.100 --> 00:53:56.160 Some of the groups were dioxin, like.

NOTE Confidence: 0.81728315

00:53:56.160 --> 00:53:58.687 I'm not, I'm not sure of any

NOTE Confidence: 0.81728315

00:53:58.687 --> 00:54:00.400 specific studies coming to mind,

NOTE Confidence: 0.81728315

 $00:54:00.400 \longrightarrow 00:54:02.320$  but it it seems likely that

NOTE Confidence: 0.81728315

 $00:54:02.320 \longrightarrow 00:54:04.280$  it may follow a similar.

NOTE Confidence: 0.81728315

 $00{:}54{:}04.280 \dashrightarrow 00{:}54{:}06.180$  Well, they're structurally similar

NOTE Confidence: 0.81728315

 $00:54:06.180 \longrightarrow 00:54:08.990$  to the other other chemicals. OK,

NOTE Confidence: 0.85703105

 $00:54:08.990 \longrightarrow 00:54:11.100$  great and then Jeffrey Townsend

00:54:11.100 --> 00:54:14.129 has a question where you do see

NOTE Confidence: 0.85703105

 $00:54:14.129 \longrightarrow 00:54:16.229$  elevated odds of thyroid cancer?

NOTE Confidence: 0.85703105

 $00:54:16.230 \longrightarrow 00:54:18.906$  Do you have any evidence discriminating

NOTE Confidence: 0.85703105

 $00:54:18.906 \longrightarrow 00:54:21.159$  between the two hypotheses of

NOTE Confidence: 0.85703105

00:54:21.159 --> 00:54:23.553 effects that occur due to hormone

NOTE Confidence: 0.85703105

 $00{:}54{:}23.553 \dashrightarrow 00{:}54{:}25.237$  disruption compared to effects

NOTE Confidence: 0.85703105

 $00:54:25.237 \longrightarrow 00:54:27.751$  that might be arising due to

NOTE Confidence: 0.85703105

00:54:27.751 --> 00:54:29.436 induction of carcinogenic mutation?

NOTE Confidence: 0.85703105

 $00:54:29.436 \longrightarrow 00:54:31.140$  Do you see ways

NOTE Confidence: 0.85703105

 $00:54:31.140 \longrightarrow 00:54:32.844$  to do this? Yeah,

NOTE Confidence: 0.85703105

 $00:54:32.844 \longrightarrow 00:54:34.548$  that's a great question.

NOTE Confidence: 0.85703105

 $00:54:34.550 \longrightarrow 00:54:36.870$  I don't really do this

NOTE Confidence: 0.85703105

 $00:54:36.870 \longrightarrow 00:54:38.726$  type of mechanistic work.

NOTE Confidence: 0.85703105

 $00:54:38.730 \longrightarrow 00:54:41.100$  I know the the thyroid hormone

NOTE Confidence: 0.85703105

00:54:41.100 --> 00:54:41.890 disruption hypothesis.

NOTE Confidence: 0.85703105

 $00:54:41.890 \longrightarrow 00:54:43.865$  There's been a lot more

 $00:54:43.865 \longrightarrow 00:54:45.840$  mechanistic work in that area,

NOTE Confidence: 0.85703105

 $00{:}54{:}45.840 \dashrightarrow 00{:}54{:}48.073$  but I'd be open to suggestions for

NOTE Confidence: 0.85703105

00:54:48.073 --> 00:54:50.090 how this could hopefully maybe

NOTE Confidence: 0.85703105

 $00:54:50.090 \longrightarrow 00:54:52.560$  inform some some mechanistic studies.

NOTE Confidence: 0.85703105

00:54:52.560 --> 00:54:54.530 I think it would be,

NOTE Confidence: 0.85703105

 $00:54:54.530 \longrightarrow 00:54:57.476$  you know, I really think that.

NOTE Confidence: 0.85703105

 $00:54:57.480 \longrightarrow 00:54:59.505$  The study could inform mechanistic

NOTE Confidence: 0.85703105

 $00:54:59.505 \longrightarrow 00:55:01.125$  work and vice versa.

NOTE Confidence: 0.85703105

 $00:55:01.130 \longrightarrow 00:55:01.540$  Yeah,

NOTE Confidence: 0.82208735

 $00:55:01.540 \longrightarrow 00:55:03.570$  that's a great great point.

NOTE Confidence: 0.82208735

 $00{:}55{:}03.570 \dashrightarrow 00{:}55{:}06.496$  And then Ashida had mentioned in regards

NOTE Confidence: 0.82208735

 $00:55:06.496 \longrightarrow 00:55:09.415$  to the policy of showing harm that

NOTE Confidence: 0.82208735

 $00{:}55{:}09.415 \dashrightarrow 00{:}55{:}12.100$  Europe does the reverse of the US.

NOTE Confidence: 0.82208735

 $00:55:12.100 \longrightarrow 00:55:14.935$  Do they see as a different trend?

NOTE Confidence: 0.8658378

 $00:55:17.560 \longrightarrow 00:55:19.044$  Actually, thyroid cancer cases

 $00:55:19.044 \longrightarrow 00:55:21.270$  are going up globally and the

NOTE Confidence: 0.8658378

 $00{:}55{:}21.336 \dashrightarrow 00{:}55{:}23.436$  trends in exposure are consistent.

NOTE Confidence: 0.8658378

00:55:23.440 --> 00:55:25.565 Actually, they were first observed

NOTE Confidence: 0.8658378

 $00{:}55{:}25.565 \dashrightarrow 00{:}55{:}28.171$  in Sweden where they have breast

NOTE Confidence: 0.8658378

00:55:28.171 --> 00:55:31.041 milk banks an they saw these flame

NOTE Confidence: 0.8658378

 $00:55:31.041 \longrightarrow 00:55:33.241$  retardants going up in human milk

NOTE Confidence: 0.8658378

 $00:55:33.241 \longrightarrow 00:55:35.552$  samples which caused a lot of alarm.

NOTE Confidence: 0.8658378

00:55:35.552 --> 00:55:38.016 At that time we didn't know if

NOTE Confidence: 0.8658378

 $00{:}55{:}38.016 \to 00{:}55{:}40.300$  they were carcinogenic or not,

NOTE Confidence: 0.8658378

 $00:55:40.300 \longrightarrow 00:55:42.701$  but given that you know babies were

NOTE Confidence: 0.8658378

 $00:55:42.701 \longrightarrow 00:55:45.779$  going to be exposed to these chemicals,

NOTE Confidence: 0.8658378

 $00:55:45.780 \longrightarrow 00:55:46.890$  that sort of.

NOTE Confidence: 0.8658378

 $00:55:46.890 \longrightarrow 00:55:48.740$  Triggered this whole area of

NOTE Confidence: 0.8658378

 $00:55:48.740 \longrightarrow 00:55:51.024$  research on these flame retardants

NOTE Confidence: 0.8658378

 $00:55:51.024 \longrightarrow 00:55:52.497$  and other chemicals.

NOTE Confidence: 0.8658378

 $00:55:52.500 \longrightarrow 00:55:52.860$  Great

 $00:55:52.860 \longrightarrow 00:55:55.756$  and then I just have one final question.

NOTE Confidence: 0.8349844

 $00{:}55{:}55.760 \dashrightarrow 00{:}55{:}58.182$  The email that we all received last

NOTE Confidence: 0.8349844

00:55:58.182 --> 00:56:00.215 week about benzene being in some

NOTE Confidence: 0.8349844

 $00:56:00.215 \longrightarrow 00:56:02.371$  of the hand sanitizers for for our

NOTE Confidence: 0.8349844

 $00:56:02.436 \longrightarrow 00:56:05.168$  COVID-19 protection? Do you have any

NOTE Confidence: 0.8349844

00:56:05.170 --> 00:56:07.342 thoughts or comments on that? Yeah,

NOTE Confidence: 0.8349844

 $00:56:07.342 \longrightarrow 00:56:10.600$  I read that I read some of the materials.

NOTE Confidence: 0.8349844

 $00:56:10.600 \longrightarrow 00:56:12.772$  I think benzene you know is

NOTE Confidence: 0.8349844

 $00:56:12.772 \longrightarrow 00:56:14.220$  a known human carcinogen.

NOTE Confidence: 0.8349844

 $00:56:14.220 \longrightarrow 00:56:16.747$  However, it is present in many sources,

NOTE Confidence: 0.8349844

 $00:56:16.750 \longrightarrow 00:56:19.319$  so I would really want to to

NOTE Confidence: 0.8349844

 $00:56:19.319 \longrightarrow 00:56:21.100$  understand how risky this is.

NOTE Confidence: 0.8349844

 $00:56:21.100 \longrightarrow 00:56:24.124$  I think we need to know how much.

NOTE Confidence: 0.8349844

 $00:56:24.130 \longrightarrow 00:56:26.377$  Benzene and how does that compare to?

NOTE Confidence: 0.8349844

00:56:26.380 --> 00:56:28.318 Like putting gasoline in your car,

00:56:28.320 --> 00:56:30.704 you know or being walking near the roadway

NOTE Confidence: 0.8349844

 $00{:}56{:}30.704 \dashrightarrow 00{:}56{:}33.466$  so I didn't raise too many alarms yet,

NOTE Confidence: 0.8349844

 $00:56:33.470 \longrightarrow 00:56:34.614$  but I would need.

NOTE Confidence: 0.8349844

00:56:34.614 --> 00:56:37.114 I feel like I need more data to

NOTE Confidence: 0.8349844

 $00:56:37.114 \longrightarrow 00:56:39.256$  be able to reach that conclusion.

NOTE Confidence: 0.8349844

00:56:39.260 --> 00:56:41.514 And I mean, the so yell health,

NOTE Confidence: 0.8349844

00:56:41.520 --> 00:56:42.808 environmental, safety and health

NOTE Confidence: 0.8349844

 $00:56:42.808 \longrightarrow 00:56:44.418$  said like let's be precautionary.

NOTE Confidence: 0.8349844

00:56:44.420 --> 00:56:46.667 Let's just get rid of these sanitizers,

NOTE Confidence: 0.8349844

00:56:46.670 --> 00:56:48.868 you know, let's let's take an action

NOTE Confidence: 0.8349844

 $00:56:48.868 \longrightarrow 00:56:50.858$  before we have all the answers,

NOTE Confidence: 0.8349844

00:56:50.860 --> 00:56:52.470 so I think that's, uh,

NOTE Confidence: 0.8349844

 $00:56:52.470 \longrightarrow 00:56:54.074$  you know, very sensible.

NOTE Confidence: 0.8349844

00:56:54.074 --> 00:56:55.277 Approach OK great.

NOTE Confidence: 0.8349844

 $00:56:55.280 \longrightarrow 00:56:55.640$  Well

NOTE Confidence: 0.803357

 $00:56:55.640 \longrightarrow 00:56:57.410$  thank you so much Dan.

 $00{:}56{:}57.410 \dashrightarrow 00{:}56{:}59.522$  Do you have any other closing

NOTE Confidence: 0.803357

 $00{:}56{:}59.522 \rightarrow 00{:}57{:}01.300$  comments? I'll just thank both

NOTE Confidence: 0.803357

 $00:57:01.300 \longrightarrow 00:57:03.418$  our speakers today. Two terrific talks.

NOTE Confidence: 0.803357

 $00{:}57{:}03.420 \dashrightarrow 00{:}57{:}05.900$  I learned alot. Thank you. Yes thank

NOTE Confidence: 0.803357

00:57:05.900 --> 00:57:10.379 you. Have a great day. Thanks.