

0:00:00 -> 0:00:02.49 Support for Yale Cancer Answers
0:00:02.49 -> 0:00:04.98 comes from AstraZeneca, dedicated
0:00:05.057 -> 0:00:07.432 to advancing options and providing
0:00:07.432 -> 0:00:10.42 hope for people living with cancer.
0:00:10.42 -> 0:00:14.38 More information at astrazeneca-us.com.
0:00:14.38 -> 0:00:16.522 Welcome to Yale Cancer Answers with
0:00:16.522 -> 0:00:18.929 your host doctor Anees Chagpar.
0:00:18.93 -> 0:00:20.81 Yale Cancer Answers features the
0:00:20.81 -> 0:00:23.111 latest information on cancer care by
0:00:23.111 -> 0:00:24.567 welcoming oncologists and specialists
0:00:24.567 -> 0:00:27.019 who are on the forefront of the
0:00:27.019 -> 0:00:28.723 battle to fight cancer. This week,
0:00:28.73 -> 0:00:30.455 it's a conversation about genetic
0:00:30.455 -> 0:00:32.18 and environmental influences in colon
0:00:32.23 -> 0:00:33.98 cancer with Doctor Caroline Johnson.
0:00:33.98 -> 0:00:35.96 Doctor Johnson is assistant professor
0:00:35.96 -> 0:00:38.341 of Epidemiology in the Department of
0:00:38.341 -> 0:00:40.041 Environmental Health Sciences at the
0:00:40.041 -> 0:00:42.367 Yale School of Public Health and Doctor
0:00:42.367 -> 0:00:44.474 Chagpar is a professor of surgical
0:00:44.48 -> 0:00:46.93 oncology at the Yale School of Medicine.
0:00:48.26 -> 0:00:50.204 Caroline you can
0:00:50.204 -> 0:00:52.634 start off by telling us
0:00:52.64 -> 0:00:55.568 a little bit about your research?
0:00:55.57 -> 0:00:58.486 I use a technology called metabolomics
0:00:58.486 -> 0:01:00.922 to investigate specific differences
0:01:00.922 -> 0:01:03.838 in metabolism that affect colon cancer,
0:01:03.84 -> 0:01:05.301 development progression and
0:01:05.301 -> 0:01:07.249 even response to therapeutics.
0:01:07.25 -> 0:01:10.165 So particularly in my research
0:01:10.165 -> 0:01:12.497 I'm interested in examining

0:01:12.5 -> 0:01:15.002 metabolism in patients that develop tumors
0:01:15.002 -> 0:01:18.406 that occur on the right side of the colon,
0:01:18.41 -> 0:01:21.443 so that is the area of the colon between
0:01:21.443 -> 0:01:24.259 the appendix and slightly up from
0:01:24.259 -> 0:01:27.47 there in the rectum and ascending colon,
0:01:27.47 -> 0:01:29.948 because those patients have the poorest
0:01:29.948 -> 0:01:32.855 survival and what we've seen in the
0:01:32.855 -> 0:01:34.825 literature is actually female patients
0:01:34.825 -> 0:01:37.122 have much higher incidence of tumors
0:01:37.122 -> 0:01:40.23 that occur in this region of the colon,
0:01:40.23 -> 0:01:43.05 so we've been using
0:01:43.05 -> 0:01:44.975 metabolomics to get a
0:01:44.975 -> 0:01:46.515 better understanding of the
0:01:46.515 -> 0:01:47.929 metabolism of these tumors.
0:01:47.93 -> 0:01:50.18 So maybe we can stop there
0:01:50.18 -> 0:01:52.952 for a second and just kind of dig a
0:01:52.952 -> 0:01:55.438 little bit deeper into what exactly
0:01:55.438 -> 0:01:58.05 metabolomics is and how that works.
0:01:59.93 -> 0:02:02.81 It's the study of all the small
0:02:02.81 -> 0:02:04.925 molecules that are present within a
0:02:04.925 -> 0:02:07.82 sample so we can take a biological sample
0:02:07.82 -> 0:02:11.18 from a patient such as a blood sample,
0:02:11.18 -> 0:02:14.26 or even a tumor tissue,
0:02:14.26 -> 0:02:17.356 and we can analyze it in an agnostic manner.
0:02:17.36 -> 0:02:19.663 So we examine basically all the different
0:02:19.663 -> 0:02:21.771 levels of all the small molecules
0:02:21.771 -> 0:02:23.883 that might be within that sample
0:02:27.68 -> 0:02:29.738 and this is similar to genomics
0:02:29.738 -> 0:02:30.424 or transcriptomics.
0:02:30.43 -> 0:02:32.15 So small molecules are basically
0:02:32.15 -> 0:02:33.87 metabolites that are within our

0:02:33.932 -> 0:02:35.834 bodies that come from the processing
0:02:35.834 -> 0:02:37.65 of things like dietary products,
0:02:37.65 -> 0:02:39.66 and they produce vital components
0:02:39.66 -> 0:02:41.67 that are needed for our bodies
0:02:41.67 -> 0:02:43.554 for different biological processes,
0:02:43.554 -> 0:02:45.909 such as growth and healing,
0:02:45.91 -> 0:02:47.323 immune responses, energy,
0:02:47.323 -> 0:02:48.736 and even sleep,
0:02:48.74 -> 0:02:51.8 so metabolomic analysis can also
0:02:51.8 -> 0:02:53.924 really show us about the metabolism
0:02:53.924 -> 0:02:56.3 of an individual and it can
0:02:56.3 -> 0:02:58.379 also show us metabolism of things
0:02:58.448 -> 0:03:00.144 like environmental chemicals and
0:03:00.144 -> 0:03:02.688 drugs as well within an individual
0:03:02.69 -> 0:03:04.628 and that could
0:03:04.628 -> 0:03:07.198 be produced by the bacteria or even
0:03:07.198 -> 0:03:09.218 the microbiome within an individual.
0:03:09.22 -> 0:03:11.675 And this technology is particularly
0:03:11.675 -> 0:03:12.657 important for cancer
0:03:12.66 -> 0:03:14.706 because we know that metabolites
0:03:14.706 -> 0:03:17.495 can affect how a tumor grows as tumor
0:03:17.495 -> 0:03:20.113 cells need nutrients and energy and the
0:03:20.113 -> 0:03:22.157 tumors themselves produce metabolites.
0:03:22.16 -> 0:03:23.89 So metabolomics can really provide
0:03:23.89 -> 0:03:26.093 us great insight into how an
0:03:26.093 -> 0:03:27.323 individual produces metabolites
0:03:27.323 -> 0:03:29.373 and how this might propagate
0:03:29.38 -> 0:03:30.9 tumor growth as well.
0:03:30.9 -> 0:03:32.04 So basically you're
0:03:32.04 -> 0:03:34.448 kind of looking at all of these
0:03:34.448 -> 0:03:36.407 metabolites to gain some insight

0:03:36.407 -> 0:03:38.115 into these colon cancers.
0:03:38.12 -> 0:03:40.318 Tell us what sample you used to
0:03:40.318 -> 0:03:42.68 to look at these metabolites.
0:03:42.68 -> 0:03:44.972 One can imagine that there may
0:03:44.972 -> 0:03:47.33 be many options that you would
0:03:47.33 -> 0:03:49.885 have whether it's looking at the stool
0:03:49.885 -> 0:03:52.679 or whether it's looking at tumor tissue,
0:03:52.68 -> 0:03:54.966 or whether it's looking at blood.
0:03:54.97 -> 0:03:58.026 So what exactly do you do to try
0:03:58.03 -> 0:03:59.554 to gain this insight?
0:03:59.554 -> 0:04:02.561 That's a really good question,
0:04:02.561 -> 0:04:05.13 basically we can take anything, we can
0:04:05.207 -> 0:04:07.958 take a blood sample or stool sample,
0:04:07.96 -> 0:04:09.344 or a tumor tissue,
0:04:09.344 -> 0:04:12.16 and we can obtain these from patients,
0:04:12.16 -> 0:04:14.736 and we can extract all the different
0:04:14.736 -> 0:04:17.578 metabolites out of these biological samples.
0:04:17.58 -> 0:04:21.01 And what we end up with is sort of a mixture
0:04:21.099 -> 0:04:24.267 of anywhere from maybe 3000 up to you
0:04:24.267 -> 0:04:27.363 know 10 to 20,000 different molecules
0:04:27.363 -> 0:04:30.687 that could be present within this
0:04:30.69 -> 0:04:33.306 sample within my research so far,
0:04:33.31 -> 0:04:35.058 we have primarily examined
0:04:35.058 -> 0:04:36.806 tumor tissues from patients,
0:04:36.81 -> 0:04:39.175 so with collaborations with
0:04:39.175 -> 0:04:41.54 both Sloan Kettering Cancer Center
0:04:41.616 -> 0:04:43.8 and also Yale Cancer Center,
0:04:43.8 -> 0:04:45.12 we obtained over
0:04:45.12 -> 0:04:47.32 200 tumor tissues from patients
0:04:47.32 -> 0:04:49.897 where these tumors had been obtained
0:04:49.897 -> 0:04:52.877 during surgery and we were able to

0:04:52.877 -> 0:04:55.739 analyze these tissues to examine which
0:04:55.739 -> 0:04:58.439 metabolites were present and how they
0:04:58.439 -> 0:05:00.554 were different between different patients.
0:05:00.56 -> 0:05:02.936 So how they were different between
0:05:02.936 -> 0:05:05.968 both women and men and from patients
0:05:05.968 -> 0:05:08.248 with right sided colorectal cancer
0:05:08.248 -> 0:05:11.26 and also from tumors that occurred in
0:05:11.26 -> 0:05:14.126 other regions of the colon as well?
0:05:14.55 -> 0:05:18.294 And if all of these patients had cancer,
0:05:18.3 -> 0:05:20.784 one would imagine that you're
0:05:20.784 -> 0:05:23.038 really looking at the metabolomic
0:05:23.038 -> 0:05:26.134 profile of tumors in these patients
0:05:26.14 -> 0:05:28.828 is that different than what you
0:05:28.828 -> 0:05:31.21 would expect in normal colon?
0:05:31.21 -> 0:05:33.45 So are there some metabolites
0:05:33.45 -> 0:05:36.243 that you would expect only in
0:05:36.243 -> 0:05:38.578 tumors versus in healthy tissue?
0:05:38.58 -> 0:05:39.969 Yeah, that's
0:05:39.97 -> 0:05:44.119 a great question, so we know that
0:05:44.12 -> 0:05:48.184 tumors have very sort of increased
0:05:48.19 -> 0:05:51.71 rapid growth, so we tend to see metabolites
0:05:51.71 -> 0:05:55.612 linked to energy metabolism and sort of
0:05:55.612 -> 0:05:58.504 making those or encouraging those building
0:05:58.504 -> 0:06:02.267 blocks to be built to build new cells so
0:06:02.267 -> 0:06:05.57 we know there's a lot of what they call
0:06:05.66 -> 0:06:08.22 metabolic rewiring that happens within
0:06:08.22 -> 0:06:12.07 a tumor compared to a normal tissue.
0:06:12.07 -> 0:06:14.04 And within my research,
0:06:14.04 -> 0:06:17.368 we were really interested in looking at the
0:06:17.368 -> 0:06:19.996 tumors themselves and how they differed
0:06:19.996 -> 0:06:22.576 between male and female patients because

0:06:22.58 -> 0:06:24.59 what is quite interesting about
0:06:24.59 -> 0:06:26.64 colorectal cancer and all cancers,
0:06:26.64 -> 0:06:28.668 they tend to have a higher
0:06:28.668 -> 0:06:30.02 incidence in male patients,
0:06:30.02 -> 0:06:32.309 but what we see is that in
0:06:32.309 -> 0:06:34.41 the right side of the colon,
0:06:34.41 -> 0:06:37.754 women tend to have this higher incidence, so
0:06:37.76 -> 0:06:40.539 we wanted to see what was different
0:06:40.539 -> 0:06:42.571 metabolically about these tumors that
0:06:42.571 -> 0:06:45.259 occur specifically in in women with right
0:06:45.259 -> 0:06:47.707 sided colorectal cancer and what we saw
0:06:47.707 -> 0:06:50.378 was that they had this very different
0:06:50.378 -> 0:06:53.054 metabolic profile where they tended to
0:06:53.06 -> 0:06:54.656 generate energy differently
0:06:54.656 -> 0:06:57.05 and they use one metabolites where
0:06:57.113 -> 0:06:59.228 they produce one metabolite school,
0:06:59.23 -> 0:07:01.588 disparaging that seemed to be much
0:07:01.588 -> 0:07:04.082 higher within this set of patients
0:07:04.082 -> 0:07:06.62 than compared to male patients that had
0:07:06.62 -> 0:07:08.432 right sided colon cancer,
0:07:08.432 -> 0:07:11.15 and also patients that had tumors
0:07:11.229 -> 0:07:13.609 in the other side of the colon.
0:07:13.61 -> 0:07:16.454 So we've really gone after this
0:07:16.454 -> 0:07:18.35 metabolic pathway to understand
0:07:18.35 -> 0:07:21.262 more about this side of metabolism and
0:07:21.262 -> 0:07:24.248 potentially how it could in the future
0:07:24.248 -> 0:07:26.328 be potentially targeted for perhaps
0:07:26.328 -> 0:07:29.077 a precision medicine approach for
0:07:29.08 -> 0:07:30.74 these groups of patients.
0:07:30.74 -> 0:07:32.815 That's interesting that
0:07:32.815 -> 0:07:35.659 women have a metabolite that

0:07:35.659 -> 0:07:38.014 processes energy differently than men.
0:07:39.804 -> 0:07:43.388 I just wonder when I think about
0:07:43.388 -> 0:07:46.509 Asparagine I started thinking about
0:07:48.493 -> 0:07:53.12 nucleic acids and amino acids
0:07:53.242 -> 0:07:57.136 that form the building blocks of
0:07:57.136 -> 0:08:01.409 cells and whether these could be
0:08:01.409 -> 0:08:05.289 manipulated based on dietary factors,
0:08:05.29 -> 0:08:06.61 for example.
0:08:06.61 -> 0:08:12.97 So when we think about how cells use energy,
0:08:12.97 -> 0:08:14.785 sometimes that may be
0:08:14.785 -> 0:08:19.02 mediated in part by people's dietary intake,
0:08:19.02 -> 0:08:21.785 did you look at that as a
0:08:21.785 -> 0:08:23.623 potential difference in male
0:08:23.623 -> 0:08:25.318 versus female patients?
0:08:25.77 -> 0:08:27.12 Within our cohort
0:08:27.12 -> 0:08:29.82 we didn't have information on diet,
0:08:29.82 -> 0:08:32.058 but that's very much something that
0:08:32.058 -> 0:08:34.758 would be useful to have something
0:08:34.758 -> 0:08:37.018 like a food frequency questionnaire,
0:08:37.02 -> 0:08:38.82 which is sometimes collected
0:08:38.82 -> 0:08:41.07 for different biobanks
0:08:41.07 -> 0:08:43.317 and in different cohorts.
0:08:43.32 -> 0:08:46.881 Yes, exactly I think it's
0:08:46.881 -> 0:08:48.629 really important here,
0:08:48.63 -> 0:08:52.014 but I think Asparagine does come from
0:08:52.014 -> 0:08:54.427 many many different dietary sources
0:08:54.427 -> 0:08:58.38 and it actually has been seen
0:08:58.38 -> 0:09:00.936 to be produced potentially,
0:09:00.94 -> 0:09:02.806 or metabolize by the microbiome as
0:09:02.806 -> 0:09:05.47 well and it can be produced internally
0:09:05.47 -> 0:09:07.725 through your own biochemical processing

0:09:07.725 -> 0:09:10.296 of other metabolites through an
0:09:10.296 -> 0:09:12.436 enzyme called Asparagine synthetase.
0:09:12.44 -> 0:09:13.29 So, biologically,
0:09:13.29 -> 0:09:16.265 it can come from your internal processing,
0:09:16.27 -> 0:09:19.678 but it can also come from dietary sources,
0:09:19.68 -> 0:09:22.23 and it can come from microbial
0:09:22.23 -> 0:09:23.505 processing as well.
0:09:23.51 -> 0:09:26.012 So, as with many metabolites that
0:09:26.012 -> 0:09:28.3 are present within
0:09:28.3 -> 0:09:31.316 tumors and also present within the colon,
0:09:31.32 -> 0:09:33.854 we always have to take into account
0:09:33.854 -> 0:09:35.392 all these different biological
0:09:35.392 -> 0:09:38.094 sources of where they can come from.
0:09:38.1 -> 0:09:40.356 So we can either
0:09:40.36 -> 0:09:42.999 manipulate them and try and sort of,
0:09:43 -> 0:09:44.131 potentially
0:09:44.131 -> 0:09:46.393 reduce the effects of the disease,
0:09:46.4 -> 0:09:47.904 or improve therapeutic response.
0:09:48.28 -> 0:09:49.04 And it seems
0:09:49.04 -> 0:09:50.845 to be so multifactorial when
0:09:50.845 -> 0:09:53.115 you think about where all of
0:09:53.115 -> 0:09:55.065 these metabolites can come from,
0:09:55.07 -> 0:09:57.566 and all of the different processes
0:09:57.566 -> 0:09:59.987 that could be going on
0:09:59.987 -> 0:10:02.222 both within normal cells as
0:10:02.222 -> 0:10:04.58 well as within cancer cells,
0:10:04.58 -> 0:10:06.368 which raises the question,
0:10:07.71 -> 0:10:10.38 do women normally have more of
0:10:10.38 -> 0:10:12.16 this metabolite even outside
0:10:12.235 -> 0:10:13.967 of their colon cancers?
0:10:14.86 -> 0:10:19.364 I think in this context what we've begun to see

0:10:19.37 -> 0:10:22.156 is that Asparagine might be increased in
0:10:22.156 -> 0:10:24.74 these patients because these tumors may be
0:10:24.74 -> 0:10:27.407 what we call nutrient deplete and this is
0:10:27.407 -> 0:10:29.895 something that we still have to look into,
0:10:29.9 -> 0:10:32.006 so we can't really confirm this,
0:10:32.01 -> 0:10:34.11 but just from our metabolomic studies,
0:10:34.11 -> 0:10:36.216 it seems to be indicating this.
0:10:36.22 -> 0:10:38.733 And this is maybe due to differences
0:10:38.733 -> 0:10:40.779 in blood supply to the tumor,
0:10:40.78 -> 0:10:41.833 or something else.
0:10:41.833 -> 0:10:43.943 Less oxygen
0:10:43.943 -> 0:10:46.4 that might be getting to the tumor.
0:10:46.4 -> 0:10:48.871 And when we look at the other
0:10:48.871 -> 0:10:50.669 processes that are going on
0:10:50.67 -> 0:10:53.337 within these samples we see
0:10:53.337 -> 0:10:55.734 that the generation of other energy
0:10:55.734 -> 0:10:58.092 metabolites is different as well,
0:10:58.1 -> 0:11:00.33 which could be indicating that
0:11:00.33 -> 0:11:02.56 there could be something particular
0:11:02.629 -> 0:11:04.735 about how these tumors might be
0:11:04.735 -> 0:11:07.09 growing in this area of the colon.
0:11:07.09 -> 0:11:09.89 So at the moment we don't have normal
0:11:09.89 -> 0:11:12.179 colon tissues from from individuals,
0:11:12.18 -> 0:11:15.05 but that's something that we do want
0:11:15.05 -> 0:11:18.625 to look at to see if
0:11:18.625 -> 0:11:21.268 the patients that do not have
0:11:21.27 -> 0:11:24.926 colon cancer, if the colon tissues have these
0:11:24.93 -> 0:11:27.275 different metabolites that
0:11:27.275 -> 0:11:30.41 could be different between men and women,
0:11:32.7 -> 0:11:35.436 and could affect the development of these tumors.
0:11:35.44 -> 0:11:38.639 You kind of wonder as

0:11:38.639 -> 0:11:41.839 well whether this is cause or effect.
0:11:41.84 -> 0:11:44.952 So in other words, is it that you
0:11:44.952 -> 0:11:48.23 had a tumor which was growing,
0:11:48.23 -> 0:11:50.278 which then caused this
0:11:50.278 -> 0:11:51.814 altered metabolomic profile,
0:11:51.82 -> 0:11:54.492 or was it that you had some other
0:11:54.492 -> 0:11:57.047 processes that were going on that
0:11:57.047 -> 0:11:58.859 altered your metabolomic profile,
0:11:58.86 -> 0:12:01.2 which then spurred on the cancer?
0:12:01.2 -> 0:12:04.328 Did you gain any insight into that question?
0:12:05.86 -> 0:12:09.94 I think it's probably more of the latter.
0:12:09.94 -> 0:12:13.51 We see that Asparagine
0:12:13.51 -> 0:12:15.55 is produced internally.
0:12:15.55 -> 0:12:18.1 As I mentioned through this
0:12:18.1 -> 0:12:19.63 enzyme asparagine synthetase,
0:12:19.63 -> 0:12:23.291 and this enzyme is controlled somewhat by
0:12:23.291 -> 0:12:26.767 another gene mutation of aging mutant Kras,
0:12:26.77 -> 0:12:31.53 so it could be that these tumors
0:12:31.53 -> 0:12:33.847 have this oncogene and it could
0:12:33.847 -> 0:12:36.009 be affecting these metabolites,
0:12:36.01 -> 0:12:39.358 so it could be an effect that we're seeing,
0:12:39.36 -> 0:12:41.598 but it is probably a combination
0:12:41.598 -> 0:12:43.836 of many things, that includes this
0:12:43.836 -> 0:12:45.696 potential mutation to this gene.
0:12:45.7 -> 0:12:48.15 But also it could be the way
0:12:48.15 -> 0:12:50.18 that the tumor is growing
0:12:50.18 -> 0:12:51.87 as I mentioned within the
0:12:51.87 -> 0:12:54.28 colon as well and all together,
0:12:54.28 -> 0:12:56.428 all these different processes are
0:12:56.428 -> 0:12:58.76 causing this effect of this increase
0:12:58.76 -> 0:13:01.916 in Asparagine that seem to help

0:13:01.92 -> 0:13:03.866 propagate the tumor when it
0:13:03.866 -> 0:13:05.766 might be under these stress
0:13:05.766 -> 0:13:08.104 conditions where it's not able to obtain
0:13:08.11 -> 0:13:10.2 nutrients in a normal fashion,
0:13:10.2 -> 0:13:13.119 so I think this is what
0:13:13.119 -> 0:13:14.37 could be happening.
0:13:14.37 -> 0:13:17.275 And also as I mentioned as well,
0:13:17.28 -> 0:13:19.44 this combination of the microbiome
0:13:19.44 -> 0:13:22.06 present as well within the colon
0:13:22.06 -> 0:13:24.364 that could be affecting how this
0:13:24.37 -> 0:13:26.46 metabolite is being processed.
0:13:29.016 -> 0:13:31.05 And it's an interesting puzzle to
0:13:31.05 -> 0:13:33.31 think about how metabolomics works
0:13:33.31 -> 0:13:36.049 along with genetic mutations and so on
0:13:36.05 -> 0:13:38.738 when we think about colon cancer.
0:13:38.74 -> 0:13:40.954 We're going to take a short
0:13:40.954 -> 0:13:43.06 break for a medical minute.
0:13:43.06 -> 0:13:45.406 Please stay tuned to learn more
0:13:45.406 -> 0:13:46.97 about genetic and environmental
0:13:47.035 -> 0:13:48.96 influences in colon cancer with
0:13:48.96 -> 0:13:50.92 my guest Doctor Caroline Johnson.
0:13:50.92 -> 0:13:53.06 Support for Yale Cancer Answers
0:13:53.06 -> 0:13:55.617 comes from AstraZeneca, working to
0:13:55.617 -> 0:13:57.997 eliminate cancer as a cause of death.
0:13:58 -> 0:14:01.528 Learn more at astrazeneca-us.com.
0:14:01.53 -> 0:14:03.36 This is a medical minute
0:14:03.36 -> 0:14:05.19 about head and neck cancers,
0:14:05.19 -> 0:14:07.434 although the percentage of oral in
0:14:07.434 -> 0:14:09.702 head and neck cancer patients in
0:14:09.702 -> 0:14:11.79 the United States is only about
0:14:11.79 -> 0:14:13.712 5% of all diagnosed cancers,

0:14:13.712 -> 0:14:15.677 there are challenging side effects
0:14:15.677 -> 0:14:17.102 associated with these types
0:14:17.102 -> 0:14:18.727 of cancer and their treatment.
0:14:18.73 -> 0:14:20.326 Clinical trials are currently
0:14:20.326 -> 0:14:22.321 underway to test innovative new
0:14:22.321 -> 0:14:24.218 treatments for head and neck cancers,
0:14:24.22 -> 0:14:26.2 and in many cases less radical
0:14:26.2 -> 0:14:28.61 surgeries are able to preserve nerves,
0:14:28.61 -> 0:14:30.806 arteries and muscles in the neck,
0:14:30.81 -> 0:14:32.45 enabling patients to move,
0:14:32.45 -> 0:14:34.912 speak, breathe and eat normally
0:14:34.912 -> 0:14:35.938 after surgery.
0:14:35.94 -> 0:14:37.992 More information is available
0:14:37.992 -> 0:14:39.018 at yalecancercenter.org.
0:14:39.02 -> 0:14:42.098 You're listening to Connecticut Public Radio.
0:14:43.28 -> 0:14:45.578 Welcome back to Yale cancer answers.
0:14:45.58 -> 0:14:48.18 This is doctor Anees Chagpar and I'm
0:14:48.18 -> 0:14:50.487 joined tonight by my guest doctor
0:14:50.487 -> 0:14:52.472 Caroline Johnson and we're talking about
0:14:52.472 -> 0:14:54.599 genetic and environmental influences in
0:14:54.599 -> 0:14:57.44 colon cancer and right before the break,
0:14:57.44 -> 0:14:59.48 Caroline was telling us about her
0:14:59.48 -> 0:15:01.33 studies looking at metabolomics.
0:15:01.33 -> 0:15:03.628 That is to say the study
0:15:03.628 -> 0:15:04.777 of different metabolites.
0:15:04.78 -> 0:15:06.316 Looking at gender differences
0:15:06.316 -> 0:15:08.236 in right sided colon cancer.
0:15:08.24 -> 0:15:10.879 So Caroline, I wanted to dig into
0:15:10.879 -> 0:15:13.87 that a little bit more because we
0:15:13.87 -> 0:15:16.095 started to talk about whether
0:15:16.1 -> 0:15:18.51 these metabolomic changes

0:15:18.51 -> 0:15:21.853 are what drives the colon cancer or
0:15:21.853 -> 0:15:24.403 whether the colon cancer is what
0:15:24.403 -> 0:15:26.949 drives the metabolomic changes,
0:15:26.95 -> 0:15:30.106 and you had mentioned that the
0:15:30.106 -> 0:15:33.185 metabolomic changes may be in part
0:15:33.185 -> 0:15:35.813 related to mutations in KRas,
0:15:35.82 -> 0:15:39.708 but we know that Kras and oncogenes
0:15:39.708 -> 0:15:43.217 may spur on cancers as well.
0:15:43.22 -> 0:15:46.268 I wonder whether these two processes
0:15:46.27 -> 0:15:48.69 are independent of each other.
0:15:48.69 -> 0:15:50.326 That is to say,
0:15:50.326 -> 0:15:52.78 Kras causes metabolomic changes and
0:15:52.864 -> 0:15:55.499 also causes separately tumor development
0:15:55.499 -> 0:15:58.85 or whether these are Interrelated.
0:15:58.85 -> 0:16:02.238 Do you have any sense on that?
0:16:03.35 -> 0:16:06.83 I think they are interrelated and the
0:16:06.83 -> 0:16:09.674 findings that we have seen
0:16:09.674 -> 0:16:12.266 linking Mutant Kras and Asparagine
0:16:12.266 -> 0:16:15.529 have been seen in other cancers as well.
0:16:15.53 -> 0:16:18.666 So you know the mutant carriers is very
0:16:18.666 -> 0:16:22.248 common in pancreatic cancers and there is a
0:16:22.25 -> 0:16:24.77 clinical trial right now
0:16:24.77 -> 0:16:26.86 actually that I saw yesterday
0:16:26.86 -> 0:16:28.532 for targeting Asparagine by
0:16:28.532 -> 0:16:30.649 using a drug
0:16:30.65 -> 0:16:33.674 along with other first line chemo.
0:16:36.36 -> 0:16:39.37 So we do know that the mutant
0:16:39.37 -> 0:16:41.26 Kras does regulate other
0:16:41.26 -> 0:16:43.36 genes and signaling pathways that
0:16:43.36 -> 0:16:45.04 does affect Asparagine production.
0:16:45.04 -> 0:16:48.064 So I think it's probably a case of mutant

0:16:48.064 -> 0:16:50.498 Kras affecting Asparagine levels.
0:16:50.5 -> 0:16:53.44 But of course, as I mentioned before,
0:16:53.44 -> 0:16:56.38 asparagine can be modulated by other sources,
0:16:59.32 -> 0:17:01.84 and also from the microbiome,
0:17:01.84 -> 0:17:04.944 and we have analyzed the microbiome from some
0:17:04.944 -> 0:17:08.557 of the tumors from the right sided patients.
0:17:08.56 -> 0:17:11.5 So from both men and women,
0:17:11.5 -> 0:17:13.7 and we have a sense that
0:17:13.7 -> 0:17:16.507 there is some microbiota
0:17:16.507 -> 0:17:18.722 that are correlated with asparagine
0:17:18.722 -> 0:17:21.963 levels only in in the female patients.
0:17:21.97 -> 0:17:25.008 So we do believe there is a
0:17:25.88 -> 0:17:27.185 multifactorial effect
0:17:27.185 -> 0:17:28.49 on asparagine production
0:17:28.49 -> 0:17:30.974 that could be itself propagating
0:17:30.974 -> 0:17:33.637 the tumors as well by giving
0:17:33.637 -> 0:17:35.02 them more nutrients,
0:17:35.02 -> 0:17:37.702 we know that Asparagine can increase
0:17:37.702 -> 0:17:41.305 the uptake of other amino acids and can
0:17:41.305 -> 0:17:44.37 affect other processes such as even
0:17:44.37 -> 0:17:45.573 polymetabolite
0:17:45.573 -> 0:17:47.177 production or autophagy,
0:17:47.18 -> 0:17:49.18 another process is like that.
0:17:49.18 -> 0:17:52.388 So I believe this is
0:17:52.39 -> 0:17:54.4 very wide combined effect.
0:17:54.4 -> 0:17:56.595 And really the technology metabolomics
0:17:56.595 -> 0:17:59.919 has allowed us to get an insight into
0:17:59.919 -> 0:18:02.82 this because we can not only
0:18:02.82 -> 0:18:03.75 analyze Asparagine,
0:18:03.75 -> 0:18:06.54 we can analyze all the other
0:18:06.54 -> 0:18:08.179 metabolites that could be

0:18:08.18 -> 0:18:10.19 affected by asparagine levels as well,
0:18:10.19 -> 0:18:12.535 it could be affected by mutant Kras
0:18:12.54 -> 0:18:14.144 so it really is
0:18:14.144 -> 0:18:17.765 a wider scope or a magnifying
0:18:17.765 -> 0:18:21.119 glass really into looking more into
0:18:21.12 -> 0:18:23.004 how these pathways are regulated
0:18:23.004 -> 0:18:25.359 by both genes and metabolites.
0:18:26.04 -> 0:18:28.416 Have you found a difference in
0:18:28.416 -> 0:18:30.537 Asparagine between men and
0:18:30.537 -> 0:18:32.357 women who are Kras negative?
0:18:32.36 -> 0:18:34.58 That is to say, they don't
0:18:34.58 -> 0:18:36.99 have a Kras mutation.
0:18:36.99 -> 0:18:39.66 I wonder whether
0:18:39.66 -> 0:18:41.95 these two are directly linked,
0:18:41.95 -> 0:18:43.321 so for example,
0:18:43.321 -> 0:18:46.52 women may have more Kras mutations,
0:18:46.52 -> 0:18:48.998 and therefore you may be seeing
0:18:48.998 -> 0:18:50.237 these metabolomic differences
0:18:50.237 -> 0:18:52.755 or whether these are really
0:18:52.755 -> 0:18:54.279 separate processes altogether?
0:18:56.23 -> 0:19:01.41 We haven't looked at that specifically
0:19:04.586 -> 0:19:07.909 but what we have done is we've
0:19:07.91 -> 0:19:09.94 looked at survival, and actually
0:19:09.94 -> 0:19:12.2 there's many different
0:19:12.2 -> 0:19:14.008 publicly available data sources
0:19:14.008 -> 0:19:17.039 that we can look at to look at gene
0:19:17.039 -> 0:19:19.268 expression and also patient survival.
0:19:19.27 -> 0:19:21.496 So we looked at mutant Kras
0:19:21.496 -> 0:19:24.149 we looked at asparagine synthetase
0:19:24.15 -> 0:19:27.43 and we saw that patients with these
0:19:27.43 -> 0:19:30.421 genes had much poorer survival if

0:19:30.421 -> 0:19:34.01 they were female and they had a right sided
0:19:34.01 -> 0:19:35.786 tumor so we compared,
0:19:35.79 -> 0:19:37.56 the Kras mutant to the Kras
0:19:37.56 -> 0:19:39.261 wild type, and it was again
0:19:39.261 -> 0:19:41.11 in these different resources
0:19:41.11 -> 0:19:43.206 we saw that it was always the female
0:19:43.206 -> 0:19:44.772 patients of right sided colon
0:19:44.772 -> 0:19:46.74 cancer that had the poorer survival,
0:19:46.74 -> 0:19:48.22 and we looked at asparagine
0:19:48.22 -> 0:19:49.7 levels within our own cohorts.
0:19:49.7 -> 0:19:52.004 And we looked at the survival data because
0:19:52.004 -> 0:19:54.43 our tumors were collected in the 1990s,
0:19:54.43 -> 0:19:56.327 so we were able to follow up
0:19:56.327 -> 0:19:57.99 with survival of the patients.
0:19:57.99 -> 0:20:00.237 And we saw that it was again,
0:20:00.24 -> 0:20:01.046 the women with
0:20:01.046 -> 0:20:03.061 right sided tumors
0:20:03.061 -> 0:20:05.03 that had poor survival,
0:20:05.03 -> 0:20:07.232 and increased risk of recurrence if
0:20:07.232 -> 0:20:09.2 they had high asparagine levels.
0:20:11.08 -> 0:20:13.32 Interesting and did you
0:20:13.32 -> 0:20:15.11 look at whether these asparagine
0:20:15.11 -> 0:20:17.396 levels were higher in tumors that
0:20:17.396 -> 0:20:20.093 were larger versus smaller, or was it
0:20:20.093 -> 0:20:22.019 if you looked at two tumors
0:20:22.019 -> 0:20:24.029 that were identical in terms
0:20:24.029 -> 0:20:26.447 of their size and their grade,
0:20:26.45 -> 0:20:28.28 and the level of invasion
0:20:28.28 -> 0:20:30.11 and their lymph node status,
0:20:30.11 -> 0:20:31.694 and all of the other markers
0:20:31.694 -> 0:20:33.756 that we look at for prognosis

0:20:33.756 -> 0:20:35.648 was asparagine independently
0:20:35.648 -> 0:20:37.43 associated with prognosis?
0:20:37.43 -> 0:20:40.034 We didn't have the size of the tumors
0:20:40.034 -> 0:20:42.14 to sort of understand that,
0:20:42.14 -> 0:20:44.12 but that's a very good question.
0:20:44.12 -> 0:20:46.86 What we did was we we had a very small
0:20:46.941 -> 0:20:49.395 amount of tumor from each patient,
0:20:49.4 -> 0:20:52 but it was the same size for each
0:20:52 -> 0:20:54.349 patient that the biopsy that we had.
0:20:54.35 -> 0:20:56.66 So we compared between those biopsy sizes.
0:20:56.66 -> 0:20:59.388 But we did take into account things like
0:20:59.388 -> 0:21:02.062 the stage of the patient and we saw
0:21:02.062 -> 0:21:04.579 across the board that it was stage one,
0:21:04.58 -> 0:21:07.226 stage two and three that had
0:21:07.23 -> 0:21:09.974 high levels of asparagine in the
0:21:09.974 -> 0:21:13.309 women with right sided colon cancer,
0:21:13.31 -> 0:21:15.212 but for men they didn't have
0:21:15.212 -> 0:21:17.041 these high levels of asparagine
0:21:17.041 -> 0:21:19.009 at these different stages,
0:21:19.01 -> 0:21:22.43 so it tended to be mostly in the
0:21:22.43 -> 0:21:23.57 women again.
0:21:23.57 -> 0:21:26.23 And so when you looked at prognosis,
0:21:26.23 -> 0:21:28.722 did you look at it and found that
0:21:28.722 -> 0:21:30.789 asparagine was correlated with prognosis?
0:21:30.79 -> 0:21:32.31 Was that independent of
0:21:32.31 -> 0:21:33.83 their stage at presentation?
0:21:34.53 -> 0:21:39.438 Yes, it seems to be
0:21:39.44 -> 0:21:41.17 independent of stages
0:21:41.17 -> 0:21:42.9 asparagine levels within the tumors.
0:21:42.9 -> 0:21:44.804 So what we really want to do
0:21:44.804 -> 0:21:47.109 next is we want to obtain blood

0:21:47.109 -> 0:21:49.233 samples from patients to see if
0:21:49.302 -> 0:21:51.547 we can measure asparagine levels.
0:21:51.55 -> 0:21:53.825 And if this could be potentially a
0:21:53.825 -> 0:21:56.048 biomarker as well for these patients.
0:21:56.05 -> 0:21:57.952 So that's something that we want
0:21:57.952 -> 0:22:00.2 to validate in a larger cohort.
0:22:00.2 -> 0:22:01.86 That's something we're looking into
0:22:01.86 -> 0:22:04.01 right now to collect these samples.
0:22:05.003 -> 0:22:06.989 When we were talking about cause
0:22:06.989 -> 0:22:09.546 versus effect, it really gets to
0:22:09.546 -> 0:22:12.144 your next steps, right?
0:22:12.144 -> 0:22:14.688 So if we think that
0:22:14.688 -> 0:22:16.899 asparagine is really an effect,
0:22:16.9 -> 0:22:20.196 in other words, you have a tumor that
0:22:20.196 -> 0:22:23.378 then causes asparagine levels to go up,
0:22:23.38 -> 0:22:25.54 such that those asparagine levels
0:22:25.54 -> 0:22:27.268 are predictive of prognosis,
0:22:27.27 -> 0:22:28.566 certainly thinking about,
0:22:28.566 -> 0:22:31.59 can we use this as a biomarker,
0:22:31.59 -> 0:22:35.542 especially if it can be found in something
0:22:35.542 -> 0:22:39.644 simple like a blood sample or a stool sample,
0:22:39.65 -> 0:22:40.946 might be helpful.
0:22:40.946 -> 0:22:42.674 On the other hand,
0:22:42.68 -> 0:22:47.01 if we think about it being more of a cause,
0:22:47.01 -> 0:22:48.466 that is to say,
0:22:48.466 -> 0:22:52.209 if you have high levels of asparagine that
0:22:52.21 -> 0:22:54.982 then sets off a cascade that leads
0:22:54.982 -> 0:22:57.838 to worse tumors and worse prognosis,
0:22:57.84 -> 0:22:59.75 then the concept might shift
0:22:59.75 -> 0:23:02.6 not only to be a biomarker,
0:23:02.6 -> 0:23:05.198 but to really think about

0:23:05.198 -> 0:23:06.93 this as a therapeutic target.
0:23:06.93 -> 0:23:11.32 So where where do you kind of come down on
0:23:11.32 -> 0:23:13.728 your next steps with regards to that?
0:23:14.51 -> 0:23:16.958 That's a really good question.
0:23:16.96 -> 0:23:18.99 We are currently designing
0:23:18.99 -> 0:23:21.899 studies to look at the effect of
0:23:21.899 -> 0:23:24.299 asparagine on tumor growth.
0:23:25.928 -> 0:23:27.963 Providing a different cell line,
0:23:27.97 -> 0:23:30.322 and animal models asparagine to see
0:23:30.322 -> 0:23:32.87 if it does propagate tumor growth.
0:23:32.87 -> 0:23:35.516 There was a study
0:23:35.516 -> 0:23:38.142 out in Nature a couple of
0:23:38.142 -> 0:23:40.841 years ago where they in a different
0:23:40.841 -> 0:23:44.285 cancer model, in a breast cancer model,
0:23:44.29 -> 0:23:44.95 they fed mice
0:23:44.95 -> 0:23:46.93 asparagine in their diet and
0:23:46.93 -> 0:23:49.257 they saw that it actually caused
0:23:49.257 -> 0:23:51.262 the primary tumor to metastasize.
0:23:51.27 -> 0:23:53.58 So there's been a number of studies
0:23:53.58 -> 0:23:55.725 that have looked into asparagine and
0:23:55.725 -> 0:23:58.77 have seen that it can propagate tumor growth.
0:23:58.77 -> 0:24:03.07 So we had we have a study that has been
0:24:03.07 -> 0:24:05.164 funded by the American Cancer Society
0:24:05.164 -> 0:24:07.968 where we will be looking at the effect
0:24:07.968 -> 0:24:10.554 of both the gene that produces
0:24:10.554 -> 0:24:12.57 asparagine so asparagine synthetase,
0:24:12.57 -> 0:24:15.258 and we've developed some cell lines where
0:24:15.258 -> 0:24:18.269 we have the knockout of this gene,
0:24:18.27 -> 0:24:22.05 and we will be
0:24:22.05 -> 0:24:24.966 injecting this
0:24:24.966 -> 0:24:28.383 into mice and also to feed them

0:24:28.383 -> 0:24:31.596 asparagine to see if it will actually
0:24:31.687 -> 0:24:34.9 affect tumor growth so
0:24:34.9 -> 0:24:37.024 hopefully in the future
0:24:37.024 -> 0:24:39.641 down the line we can sort of test
0:24:39.641 -> 0:24:42.284 to see if any of the asparagine
0:24:42.284 -> 0:24:44.509 reducing drugs
0:24:44.509 -> 0:24:47.31 could be used as a therapeutic
0:24:47.31 -> 0:24:49.135 to reduce asparagine levels
0:24:49.14 -> 0:24:51.326 in colon cancer patients, potentially.
0:24:52.06 -> 0:24:54.98 it's so interesting when you talk about that
0:24:54.98 -> 0:24:57.318 study in breast cancer where feeding
0:24:57.318 -> 0:24:59.72 asparagine led to increased metastasis.
0:24:59.72 -> 0:25:02.443 One of the obvious questions I'm sure
0:25:02.443 -> 0:25:05.797 all of our listeners want to know is
0:25:05.8 -> 0:25:10.128 what foods out there are high in asparagine?
0:25:11.37 -> 0:25:13.055 That's something
0:25:13.055 -> 0:25:14.74 we're looking into as well.
0:25:14.74 -> 0:25:17.764 As with any sort of food source,
0:25:17.77 -> 0:25:19.455 there are many different components
0:25:19.455 -> 0:25:21.448 within a
0:25:21.448 -> 0:25:23.893 vegetable or within
0:25:23.893 -> 0:25:26.734 anything that you eat.
0:25:29.3 -> 0:25:32.63 I think if it was going to be given
0:25:32.63 -> 0:25:36.05 as a therapeutic
0:25:36.05 -> 0:25:38.946 I don't know if diet is
0:25:38.946 -> 0:25:41.736 really the best way to approach it.
0:25:41.74 -> 0:25:44.008 It could be better to potentially
0:25:44.008 -> 0:25:45.142 try and reduce
0:25:45.15 -> 0:25:46.32 asparagine levels,
0:25:46.32 -> 0:25:49.492 and that's what I mean as using
0:25:49.492 -> 0:25:52.075 it as a preventative measure

0:25:52.075 -> 0:25:54.342 so encouraging people to eat less
0:25:54.342 -> 0:25:56.52 foods that are high in asparagine.
0:25:56.52 -> 0:25:58.415 Which brings us to the
0:25:58.415 -> 0:26:00.31 question which foods are those?
0:26:03.77 -> 0:26:06.038 At the moment we don't really know
0:26:06.038 -> 0:26:08.538 which foods have high asparagine levels.
0:26:08.54 -> 0:26:10.532 That's something that we
0:26:10.532 -> 0:26:13.333 would need to look into 'cause you know
0:26:13.333 -> 0:26:15.439 each food product does contain many
0:26:15.507 -> 0:26:18.075 different amino acids and other products,
0:26:18.08 -> 0:26:20.564 and it tends to be some food products that
0:26:20.564 -> 0:26:23.26 may have higher asparagine levels have
0:26:23.26 -> 0:26:25.79 other beneficial properties.
0:26:28.05 -> 0:26:29.838 Yeah, that's a
0:26:29.838 -> 0:26:31.179 really interesting point,
0:26:31.18 -> 0:26:33.286 but I think that perhaps
0:26:33.286 -> 0:26:35.839 targeting maybe
0:26:35.839 -> 0:26:37.975 a therapeutic standpoint from
0:26:37.975 -> 0:26:40.111 using something like asparagine.
0:26:40.12 -> 0:26:42.796 AIDS might perhaps be more effective,
0:26:42.8 -> 0:26:45.458 but definitely the diet would be
0:26:45.458 -> 0:26:47.753 something that would be useful
0:26:47.753 -> 0:26:50.399 to look into for these patients.
0:26:50.4 -> 0:26:53.034 Yeah, because they kind of wonder
0:26:53.034 -> 0:26:54.79 whether women just naturally
0:26:54.865 -> 0:26:56.817 gravitate towards eating foods
0:26:56.817 -> 0:26:59.257 that are higher in asparagine
0:26:59.26 -> 0:27:02.506 or whether they process those
0:27:02.506 -> 0:27:06.299 differently such that they end up with
0:27:06.299 -> 0:27:09.365 higher levels of asparagine versus men,
0:27:09.37 -> 0:27:12.278 and so understanding how

0:27:12.278 -> 0:27:15.186 they metabolize those foods
0:27:15.19 -> 0:27:17.962 might play a role, but can you
0:27:17.962 -> 0:27:21.367 comment that in looking at the
0:27:21.367 -> 0:27:23.887 enzymes that breakdown asparagine and
0:27:23.887 -> 0:27:26.747 also those that increase asparagine ,
0:27:26.75 -> 0:27:29.878 did you find a difference between men and
0:27:29.878 -> 0:27:33.168 women in terms of their natural enzymes?
0:27:33.17 -> 0:27:35.726 Even outside of the cancer patient?
0:27:35.73 -> 0:27:37.45 We haven't looked at
0:27:37.45 -> 0:27:39.59 the expression levels of those,
0:27:39.59 -> 0:27:42.579 but that's a really interesting point.
0:27:42.58 -> 0:27:45.639 We do know that the asparagine synthetase
0:27:45.64 -> 0:27:47.986 is associated with poor survival
0:27:47.99 -> 0:27:50.646 if it's a higher expression only in
0:27:50.646 -> 0:27:53.479 women with right sided colorectal cancer.
0:27:53.48 -> 0:27:55.872 But I think also having a
0:27:55.872 -> 0:27:58.031 look more deeply at the microbiome
0:27:58.031 -> 0:28:00.835 because we know that there are many
0:28:00.835 -> 0:28:03.28 species within the microbiome that
0:28:03.28 -> 0:28:05.236 can also metabolize asparagine.
0:28:05.24 -> 0:28:07.2 This could be, you know,
0:28:07.2 -> 0:28:08.768 another therapeutic that
0:28:08.768 -> 0:28:10.728 could be explored as well,
0:28:10.73 -> 0:28:13.166 and I think having a
0:28:13.166 -> 0:28:15.649 more in depth look at
0:28:15.65 -> 0:28:17.53 the microbiome that could be
0:28:17.53 -> 0:28:19.842 present within the stool sample or
0:28:19.842 -> 0:28:21.687 within the tissue samples within
0:28:21.687 -> 0:28:23.86 patients is also really important.
0:28:25.03 -> 0:28:27.196 The other question
0:28:27.196 -> 0:28:29.946 that comes to mind is while your

0:28:29.946 -> 0:28:32.406 research is really focused on the
0:28:32.406 -> 0:28:34.418 differences between men and women,
0:28:34.42 -> 0:28:36.43 one wonders, especially when you
0:28:36.43 -> 0:28:38.877 think about the potential role for
0:28:38.877 -> 0:28:41.067 asparagine in mediating prognosis.
0:28:41.07 -> 0:28:43.597 I'm going back to that study
0:28:43.597 -> 0:28:46.607 that you said was published in Nature
0:28:46.61 -> 0:28:49.426 in the breast cancer model,
0:28:49.43 -> 0:28:51.548 whether if you look at
0:28:51.548 -> 0:28:52.96 men with colon cancers,
0:28:52.96 -> 0:28:54.675 whether men with higher levels
0:28:54.675 -> 0:28:56.814 of asparagine do worse than men
0:28:56.814 -> 0:28:58.609 with lower levels of asparagine
0:28:58.61 -> 0:29:00.38 have you looked at that?
0:29:00.38 -> 0:29:02.14 We have and it doesn't
0:29:02.14 -> 0:29:03.91 seem to be the case,
0:29:03.91 -> 0:29:06.781 so it seems to be sort of what we've
0:29:06.781 -> 0:29:09.906 seen is the opposite way round.
0:29:09.91 -> 0:29:11.752 The with you for male patient
0:29:11.752 -> 0:29:13.79 has higher levels of disparaging.
0:29:13.79 -> 0:29:15.56 They tend to do better.
0:29:15.56 -> 0:29:18.176 So it's really perplexing
0:29:18.18 -> 0:29:19.044 Interesting, you know,
0:29:19.044 -> 0:29:20.196 and it's really fascinating,
0:29:20.2 -> 0:29:21.904 so it's something that you know
0:29:21.904 -> 0:29:23.388 where we're looking into within
0:29:23.388 -> 0:29:24.828 my lab in different models,
0:29:24.83 -> 0:29:26.558 so hopefully we'll get
0:29:26.56 -> 0:29:28.702 better insight into this in the
0:29:28.702 -> 0:29:30.61 the next couple of years or so.
0:29:31.29 -> 0:29:33.215 Doctor Caroline Johnson is assistant

0:29:33.215 -> 0:29:35.564 professor of Epidemiology in the Department
0:29:35.564 -> 0:29:37.379 of Environmental Health Sciences at
0:29:37.379 -> 0:29:39.67 the Yale School of Public Health.
0:29:39.67 -> 0:29:41.202 If you have questions,
0:29:41.202 -> 0:29:42.734 the address is canceranswers@yale.edu
0:29:42.734 -> 0:29:44.843 and past editions of the program
0:29:44.843 -> 0:29:46.775 are available in audio and written
0:29:46.83 -> 0:29:48.438 form at yalecancercenter.org.
0:29:48.44 -> 0:29:51.216 We hope you'll join us next week to
0:29:51.216 -> 0:29:53.925 learn more about the fight against
0:29:53.925 -> 0:29:56.823 cancer here on Connecticut Public Radio.