WEBVTT

NOTE duration: ”00:04:22.912”

NOTE Confidence: 0.9299307

00:00:04.880 --> 00:00:06.980 DNA pulls our genomic information,

NOTE Confidence: 0.903482

00:00:07.440 --> 00:00:08.260 and unfortunately,

NOTE Confidence: 0.9459559

00:00:08.800 --> 00:00:10.320 it's not inert and it's

NOTE Confidence: 0.9459559

00:00:10.320 --> 00:00:11.940 subject to damage.

NOTE Confidence: 0.9949858

00:00:12.905 --> 00:00:14.105 Because we want to be

NOTE Confidence: 0.9949858

00:00:14.105 --> 00:00:15.965 able to preserve our genomic

NOTE Confidence: 0.9949858

00:00:16.025 --> 00:00:16.525 information,

NOTE Confidence: 0.9792707

00:00:16.905 --> 00:00:18.585 cells have evolved this very

NOTE Confidence: 0.9792707

00:00:18.585 --> 00:00:20.825 intricate system called DNA damage

NOTE Confidence: 0.9792707

00:00:20.825 --> 00:00:21.325 response.

NOTE Confidence: 0.99513125

00:00:21.785 --> 00:00:23.085 And there are two main

NOTE Confidence: 0.99513125

00:00:23.145 --> 00:00:23.645 pathways

NOTE Confidence: 0.9840646

00:00:24.025 --> 00:00:25.645 that happen within the system,

NOTE Confidence: 0.9840646

00:00:25.864 --> 00:00:26.765 DNA repair

NOTE Confidence: 0.9915571

00:00:28.179 --> 00:00:28.920 and apoptosis.

NOTE Confidence: 0.9761766

00:00:30.099 --> 00:00:31.859 So if a cell has

NOTE Confidence: 0.9761766

00:00:31.859 --> 00:00:33.780 DNA damage, it can choose

NOTE Confidence: 0.9761766

00:00:33.780 --> 00:00:35.879 to use many different mechanisms

NOTE Confidence: 0.9761766

00:00:36.020 --> 00:00:37.320 to repair that damage.

NOTE Confidence: 0.9899704

00:00:37.699 --> 00:00:39.315 But in cases when there's

NOTE Confidence: 0.9899704

00:00:39.395 --> 00:00:41.155 so much damage, the cell

NOTE Confidence: 0.9899704

00:00:41.155 --> 00:00:42.914 might decide it's in their

NOTE Confidence: 0.9899704

00:00:42.914 --> 00:00:45.094 best interest to activate apoptosis

NOTE Confidence: 0.8744286

00:00:45.475 --> 00:00:46.835 or in other words, its

NOTE Confidence: 0.8744286

00:00:46.835 --> 00:00:47.815 own cell death.

NOTE Confidence: 0.980361

00:00:52.515 --> 00:00:54.214 My lab is really interested

NOTE Confidence: 0.980361

00:00:54.274 --> 00:00:56.370 in trying to understand how

NOTE Confidence: 0.980361

00:00:56.370 --> 00:00:58.290 pathways within the DNA damage

NOTE Confidence: 0.980361

00:00:58.290 --> 00:00:59.910 response talk to each other.

NOTE Confidence: 0.9879769

00:01:00.610 --> 00:01:02.790 We have a specific interest

NOTE Confidence: 0.9879769

00:01:02.930 --> 00:01:04.709 in altered DNA structures.

NOTE Confidence: 0.94725597

00:01:05.250 --> 00:01:07.810 So DNA, primarily the structure

NOTE Confidence: 0.94725597

00:01:07.810 --> 00:01:09.330 is a duplex, meaning it

NOTE Confidence: 0.94725597

00:01:09.330 --> 00:01:10.755 is comprised of two different

NOTE Confidence: 0.94725597

00:01:10.755 --> 00:01:11.815 strands of DNA.

NOTE Confidence: 0.99288833

00:01:12.194 --> 00:01:13.415 But under some biological

NOTE Confidence: 0.99074054

00:01:13.795 --> 00:01:14.295 processes,

NOTE Confidence: 0.99625635

00:01:14.834 --> 00:01:16.755 cells can actually form altered

NOTE Confidence: 0.99625635

00:01:16.755 --> 00:01:18.194 structures that are different from

NOTE Confidence: 0.99625635

00:01:18.194 --> 00:01:18.935 this duplex.

NOTE Confidence: 0.95311517

00:01:19.635 --> 00:01:21.075 Our lab is focusing on

NOTE Confidence: 0.95311517

00:01:21.075 --> 00:01:22.055 triplex DNA.

NOTE Confidence: 0.98381776

00:01:22.355 --> 00:01:23.659 So that means that instead

NOTE Confidence: 0.98381776

00:01:23.659 --> 00:01:24.780 of having two strands of

NOTE Confidence: 0.98381776

00:01:24.780 --> 00:01:26.459 DNA, the cell then has

NOTE Confidence: 0.98381776

00:01:26.459 --> 00:01:27.759 three strands of DNA.

NOTE Confidence: 0.98708314

00:01:28.140 --> 00:01:30.159 And that three stranded structure

NOTE Confidence: 0.98708314

00:01:30.299 --> 00:01:31.979 is actually recognized by the

NOTE Confidence: 0.98708314

00:01:31.979 --> 00:01:33.819 cell as DNA damage. And

NOTE Confidence: 0.98708314

00:01:33.819 --> 00:01:35.119 we are trying to understand

NOTE Confidence: 0.94533473

00:01:35.500 --> 00:01:37.520 what proteins involved in repair

NOTE Confidence: 0.95065236

00:01:38.435 --> 00:01:40.755 actually are also essential for

NOTE Confidence: 0.95065236

00:01:40.755 --> 00:01:42.675 determining that repair can be

NOTE Confidence: 0.95065236

00:01:42.675 --> 00:01:43.175 efficient.

NOTE Confidence: 0.9944639

00:01:43.635 --> 00:01:45.175 We now need to incorporate

NOTE Confidence: 0.9944639

00:01:45.315 --> 00:01:46.375 and alert

NOTE Confidence: 0.9981199

00:01:46.675 --> 00:01:47.175 apoptosis

NOTE Confidence: 0.9769346

00:01:47.555 --> 00:01:48.755 that it needs to step

NOTE Confidence: 0.9769346

00:01:48.755 --> 00:01:50.354 in in order to preserve

NOTE Confidence: 0.9769346

00:01:50.354 --> 00:01:51.415 genomic integrity.

NOTE Confidence: 0.99588203

00:01:57.190 --> 00:01:59.110 My lab is really using

NOTE Confidence: 0.99588203

00:01:59.110 --> 00:02:01.050 molecular biology and biochemistry

NOTE Confidence: 0.99670786

00:02:01.430 --> 00:02:03.050 techniques to try and understand

NOTE Confidence: 0.99670786

00:02:03.110 --> 00:02:04.090 repair proteins.

NOTE Confidence: 0.9940081

00:02:04.595 --> 00:02:06.515 We use microscopy to look

NOTE Confidence: 0.9940081

00:02:06.515 --> 00:02:07.715 at these proteins on a

NOTE Confidence: 0.9940081

00:02:07.715 --> 00:02:08.915 cellular level and to see

NOTE Confidence: 0.9940081

00:02:08.915 --> 00:02:09.955 where they go within the

NOTE Confidence: 0.9940081

00:02:09.955 --> 00:02:12.115 cell. We also use those

NOTE Confidence: 0.9940081

00:02:12.115 --> 00:02:14.135 microscopy techniques to be able

NOTE Confidence: 0.9940081

00:02:14.275 --> 00:02:15.014 to understand

NOTE Confidence: 0.99115235

00:02:15.475 --> 00:02:16.995 where the DNA damage is,

NOTE Confidence: 0.99115235

00:02:16.995 --> 00:02:18.275 how the damage is getting

NOTE Confidence: 0.99115235

00:02:18.275 --> 00:02:18.775 repaired

NOTE Confidence: 0.9883642

00:02:19.169 --> 00:02:20.370 and we look at this

NOTE Confidence: 0.9883642

00:02:20.370 --> 00:02:21.889 in many different cancer cell

NOTE Confidence: 0.9883642

00:02:21.889 --> 00:02:23.489 lines, in many different cancer

NOTE Confidence: 0.9883642

00:02:23.489 --> 00:02:25.010 types. In particular, my lab

NOTE Confidence: 0.9883642

00:02:25.010 --> 00:02:25.669 is interested

NOTE Confidence: 0.99763304

00:02:26.049 --> 00:02:28.150 in breast cancer and ovarian

NOTE Confidence: 0.99763304

00:02:28.290 --> 00:02:28.790 cancer.

NOTE Confidence: 0.984875

00:02:29.730 --> 00:02:31.329 In addition to looking at

NOTE Confidence: 0.984875

00:02:31.329 --> 00:02:33.109 things on a microscopic level,

NOTE Confidence: 0.984875

00:02:33.215 --> 00:02:34.814 we're also interested in looking

NOTE Confidence: 0.984875

00:02:34.814 --> 00:02:36.014 at things from a genomic

NOTE Confidence: 0.984875

00:02:36.014 --> 00:02:37.775 level. So we do bulk

NOTE Confidence: 0.984875

00:02:37.775 --> 00:02:39.855 RNA sequencing and looking at

NOTE Confidence: 0.984875

00:02:39.855 --> 00:02:41.694 different genomic techniques so that

NOTE Confidence: 0.984875

00:02:41.694 --> 00:02:43.454 we can actually see where

NOTE Confidence: 0.984875

00:02:43.454 --> 00:02:45.055 in the genome across the

NOTE Confidence: 0.984875

00:02:45.055 --> 00:02:46.334 whole entire cell is this

NOTE Confidence: 0.984875

00:02:46.334 --> 00:02:47.235 damage happening.

NOTE Confidence: 0.9786376

00:02:52.220 --> 00:02:53.820 There are several different types

NOTE Confidence: 0.9786376

00:02:53.820 --> 00:02:55.740 of cancers, and one type

NOTE Confidence: 0.9786376

00:02:55.740 --> 00:02:57.100 of cancer are cancers that

NOTE Confidence: 0.9786376

00:02:57.100 --> 00:02:58.160 have gene amplification.

NOTE Confidence: 0.99091184

00:02:58.700 --> 00:02:59.980 And so what that means

NOTE Confidence: 0.99091184

00:02:59.980 --> 00:03:01.660 is that the cell has

NOTE Confidence: 0.99091184

00:03:01.660 --> 00:03:03.014 determined that in order for

NOTE Confidence: 0.99091184

00:03:03.014 --> 00:03:04.715 it to grow very aggressively,

NOTE Confidence: 0.9837919

00:03:05.095 --> 00:03:07.175 it will have multiple copies

NOTE Confidence: 0.9837919

00:03:07.175 --> 00:03:08.535 of a gene, and that

NOTE Confidence: 0.9837919

00:03:08.535 --> 00:03:09.895 gene gives it the growth

NOTE Confidence: 0.9837919

00:03:09.895 --> 00:03:10.395 advantage.

NOTE Confidence: 0.99724716

00:03:11.014 --> 00:03:11.514 Traditionally,

NOTE Confidence: 0.98157656

00:03:11.975 --> 00:03:14.215 drug development strategies have been

NOTE Confidence: 0.98157656

00:03:14.215 --> 00:03:16.230 to target those over expressed

NOTE Confidence: 0.98157656

00:03:16.290 --> 00:03:17.970 protein products that happen as

NOTE Confidence: 0.98157656

00:03:17.970 --> 00:03:19.510 a result of the amplified

NOTE Confidence: 0.98157656

00:03:19.570 --> 00:03:21.330 genes. This has been very

NOTE Confidence: 0.98157656

00:03:21.330 --> 00:03:22.770 powerful, but it has been

NOTE Confidence: 0.98157656

00:03:22.770 --> 00:03:24.450 a limiting factor for many

NOTE Confidence: 0.98157656

00:03:24.450 --> 00:03:26.150 other types of cancers where

NOTE Confidence: 0.98157656

00:03:26.290 --> 00:03:28.050 small molecule targeting of those

NOTE Confidence: 0.98157656

00:03:28.050 --> 00:03:29.970 proteins is not effective and

NOTE Confidence: 0.98157656

00:03:29.970 --> 00:03:30.585 it's not

NOTE Confidence: 0.9907148

00:03:31.385 --> 00:03:32.425 doable. And so what my

NOTE Confidence: 0.9907148

00:03:32.425 --> 00:03:33.865 lab has been doing is

NOTE Confidence: 0.9907148

00:03:33.865 --> 00:03:35.385 to find ways to really

NOTE Confidence: 0.9907148

00:03:35.385 --> 00:03:36.905 target these cancers on a

NOTE Confidence: 0.9907148

00:03:36.905 --> 00:03:37.885 genomic level.

NOTE Confidence: 0.9121073

00:03:38.745 --> 00:03:40.685 We can design these synthetic

NOTE Confidence: 0.9121073

00:03:40.825 --> 00:03:41.325 oligonucleotide

NOTE Confidence: 0.96321005

00:03:42.025 --> 00:03:44.685 molecules that bind sequence specifically

NOTE Confidence: 0.96321005

00:03:44.825 --> 00:03:46.740 to the amplified gene. This

NOTE Confidence: 0.96321005

00:03:46.740 --> 00:03:48.120 creates a triplet structure.

NOTE Confidence: 0.9924896

00:03:48.500 --> 00:03:49.640 We know that the triplet

NOTE Confidence: 0.9924896

00:03:49.700 --> 00:03:51.140 structures, if you have enough

NOTE Confidence: 0.9924896

00:03:51.140 --> 00:03:53.060 of them formed, can cause

NOTE Confidence: 0.9924896

00:03:53.060 --> 00:03:54.340 the cell and force the

NOTE Confidence: 0.9924896

00:03:54.340 --> 00:03:56.180 cancer cell to activate its

NOTE Confidence: 0.9924896

00:03:56.180 --> 00:03:57.000 own death.

NOTE Confidence: 0.98630637

00:03:57.300 --> 00:03:58.900 We can use this system

NOTE Confidence: 0.98630637

00:03:58.900 --> 00:04:00.980 of manipulating DNA repair and

NOTE Confidence: 0.98630637

00:04:00.980 --> 00:04:01.480 apoptosis

NOTE Confidence: 0.99694926

00:04:01.845 --> 00:04:03.205 to cause cancer cells to

NOTE Confidence: 0.99694926

00:04:03.205 --> 00:04:03.705 die.

NOTE Confidence: 0.9790821

00:04:04.005 --> 00:04:05.205 I think it has far

NOTE Confidence: 0.9790821

00:04:05.205 --> 00:04:06.185 reaching amplifications

NOTE Confidence: 0.97098684

00:04:06.885 --> 00:04:08.005 because there are over four

NOTE Confidence: 0.97098684

00:04:08.005 --> 00:04:09.365 hundred and fifty genes that

NOTE Confidence: 0.97098684

00:04:09.365 --> 00:04:11.305 are amplified within cancer cells

NOTE Confidence: 0.97098684

00:04:11.445 --> 00:04:12.805 in more than over fourteen

NOTE Confidence: 0.97098684

00:04:12.805 --> 00:04:14.826 subtypes of cancer. So this

NOTE Confidence: 0.97098684

00:04:14.826 --> 00:04:16.746 platform has really broad reaching

NOTE Confidence: 0.97098684

00:04:16.746 --> 00:04:17.246 applications.