

WEBVTT

NOTE duration: "00:04:11.477"

NOTE Confidence: 0.98699176

00:00:05.040 --> 00:00:06.580 Cell death is a key

NOTE Confidence: 0.98699176

00:00:06.640 --> 00:00:08.639 process that's necessary even in

NOTE Confidence: 0.98699176

00:00:08.639 --> 00:00:10.000 development in order to get

NOTE Confidence: 0.98699176

00:00:10.000 --> 00:00:11.300 a viable organism.

NOTE Confidence: 0.96776295

00:00:13.039 --> 00:00:14.719 This program is called upon

NOTE Confidence: 0.96776295

00:00:14.719 --> 00:00:15.975 again over and over in

NOTE Confidence: 0.96776295

00:00:16.055 --> 00:00:17.655 in almost every disease I

NOTE Confidence: 0.96776295

00:00:17.655 --> 00:00:19.335 can think of, where you

NOTE Confidence: 0.96776295

00:00:19.335 --> 00:00:21.255 either have diseases where there's

NOTE Confidence: 0.96776295

00:00:21.255 --> 00:00:23.015 too little cell death, such

NOTE Confidence: 0.96776295

00:00:23.015 --> 00:00:23.915 as in cancer,

NOTE Confidence: 0.98782504

00:00:25.175 --> 00:00:26.454 or you have diseases where

NOTE Confidence: 0.98782504

00:00:26.454 --> 00:00:27.895 there's too much cell death,

NOTE Confidence: 0.98782504

00:00:27.895 --> 00:00:29.494 such as in strokes or

NOTE Confidence: 0.98782504

00:00:29.494 --> 00:00:30.315 heart attacks.
NOTE Confidence: 0.95352143

00:00:35.360 --> 00:00:36.720 My lab is very interested
NOTE Confidence: 0.95352143

00:00:36.720 --> 00:00:38.080 in the process of cell
NOTE Confidence: 0.95352143

00:00:38.080 --> 00:00:39.860 death. That is how cells
NOTE Confidence: 0.95352143

00:00:40.159 --> 00:00:41.600 no longer survive. What are
NOTE Confidence: 0.95352143

00:00:41.600 --> 00:00:43.280 the things that cause them
NOTE Confidence: 0.95352143

00:00:43.280 --> 00:00:44.159 to die and then what
NOTE Confidence: 0.95352143

00:00:44.159 --> 00:00:46.159 are the molecular pathways by
NOTE Confidence: 0.95352143

00:00:46.159 --> 00:00:47.055 which they can die?
NOTE Confidence: 0.9960895

00:00:48.575 --> 00:00:49.695 So if we can determine
NOTE Confidence: 0.9960895

00:00:49.695 --> 00:00:51.055 the pathway by which those
NOTE Confidence: 0.9960895

00:00:51.055 --> 00:00:52.575 cells are being forced to
NOTE Confidence: 0.9960895

00:00:52.575 --> 00:00:54.655 die, we can then prevent
NOTE Confidence: 0.9960895

00:00:54.655 --> 00:00:56.255 that death and maintain the
NOTE Confidence: 0.9960895

00:00:56.255 --> 00:00:57.715 function of those cells.
NOTE Confidence: 0.9761925

00:01:01.380 --> 00:01:02.579 There are multiple different types

NOTE Confidence: 0.9761925
00:01:02.579 --> 00:01:03.860 of death pathways that one
NOTE Confidence: 0.9761925
00:01:03.860 --> 00:01:04.360 could,
NOTE Confidence: 0.9801003
00:01:04.819 --> 00:01:06.180 attack. We look at two
NOTE Confidence: 0.9801003
00:01:06.180 --> 00:01:08.100 in particular. One is the
NOTE Confidence: 0.9801003
00:01:08.100 --> 00:01:10.120 intrinsic pathway of apoptosis,
NOTE Confidence: 0.9756157
00:01:10.819 --> 00:01:12.340 which is mediated by a
NOTE Confidence: 0.9756157
00:01:12.340 --> 00:01:14.120 family of genes called BCL2
NOTE Confidence: 0.8789091
00:01:14.500 --> 00:01:15.479 family members,
NOTE Confidence: 0.91460156
00:01:15.780 --> 00:01:17.194 one of which we study
NOTE Confidence: 0.91460156
00:01:17.194 --> 00:01:18.955 that's really poorly understood is
NOTE Confidence: 0.91460156
00:01:18.955 --> 00:01:20.635 called BOC or b o
NOTE Confidence: 0.91460156
00:01:20.635 --> 00:01:21.135 k.
NOTE Confidence: 0.85332114
00:01:21.915 --> 00:01:22.415 BOC,
NOTE Confidence: 0.96519053
00:01:22.875 --> 00:01:24.235 unlike all the other BCL
NOTE Confidence: 0.96519053
00:01:24.235 --> 00:01:25.595 two family members which primarily
NOTE Confidence: 0.96519053

00:01:25.595 --> 00:01:27.035 act at the mitochondria, acts
NOTE Confidence: 0.96519053

00:01:27.035 --> 00:01:28.955 at the endoplasmic reticulum or
NOTE Confidence: 0.96519053

00:01:28.955 --> 00:01:29.775 the ER.
NOTE Confidence: 0.966527

00:01:30.569 --> 00:01:32.569 BAC is important for ER
NOTE Confidence: 0.966527

00:01:32.569 --> 00:01:33.069 stress,
NOTE Confidence: 0.95365494

00:01:33.929 --> 00:01:35.289 agents, and there are many
NOTE Confidence: 0.95365494

00:01:35.289 --> 00:01:37.469 different diseases which involve
NOTE Confidence: 0.85917324

00:01:37.850 --> 00:01:39.770 ER stress and or invoke
NOTE Confidence: 0.85917324

00:01:39.770 --> 00:01:40.750 it. And,
NOTE Confidence: 0.98610216

00:01:41.289 --> 00:01:41.789 tauopathies
NOTE Confidence: 0.9760259

00:01:42.329 --> 00:01:44.189 are one in particular because
NOTE Confidence: 0.9760259

00:01:44.250 --> 00:01:45.785 in this form of neurodegeneration,
NOTE Confidence: 0.9733506

00:01:46.725 --> 00:01:48.805 there's an overproduction of this
NOTE Confidence: 0.9733506

00:01:48.805 --> 00:01:51.545 protein tau, which then forms
NOTE Confidence: 0.9733506

00:01:51.765 --> 00:01:52.265 oligomers
NOTE Confidence: 0.96832615

00:01:52.885 --> 00:01:54.325 and causes a lot of

NOTE Confidence: 0.96832615
00:01:54.325 --> 00:01:55.145 ER stress.
NOTE Confidence: 0.9947751
00:01:55.605 --> 00:01:56.985 And as the name neurodegeneration
NOTE Confidence: 0.9974272
00:01:57.445 --> 00:01:57.945 implies,
NOTE Confidence: 0.99204504
00:01:58.300 --> 00:01:59.740 the main feature we see
NOTE Confidence: 0.99204504
00:01:59.740 --> 00:02:01.580 is loss of neurons, so
NOTE Confidence: 0.99204504
00:02:01.580 --> 00:02:02.080 death.
NOTE Confidence: 0.9968175
00:02:03.020 --> 00:02:04.860 If we learn exactly how
NOTE Confidence: 0.9968175
00:02:04.860 --> 00:02:06.380 Bach is mediating cell death
NOTE Confidence: 0.9968175
00:02:06.380 --> 00:02:07.600 within these neurons,
NOTE Confidence: 0.988863
00:02:07.900 --> 00:02:09.260 then perhaps we can find
NOTE Confidence: 0.988863
00:02:09.260 --> 00:02:10.319 a way to inhibit
NOTE Confidence: 0.9974061
00:02:10.860 --> 00:02:12.780 Bach's action and keep these
NOTE Confidence: 0.9974061
00:02:12.780 --> 00:02:13.760 neurons alive.
NOTE Confidence: 0.98397464
00:02:16.435 --> 00:02:18.435 The second way is the
NOTE Confidence: 0.98397464
00:02:18.435 --> 00:02:20.595 extrinsic pathway of cell death.
NOTE Confidence: 0.98397464

00:02:20.595 --> 00:02:23.075 That's where other cells are
NOTE Confidence: 0.98397464

00:02:23.075 --> 00:02:24.835 from the outside causing the
NOTE Confidence: 0.98397464

00:02:24.835 --> 00:02:26.294 death of the cells.
NOTE Confidence: 0.9392378

00:02:26.860 --> 00:02:28.300 So often in the immune
NOTE Confidence: 0.9392378

00:02:28.300 --> 00:02:29.820 system, T cells are known
NOTE Confidence: 0.9392378

00:02:29.820 --> 00:02:31.260 as killers. They kill other
NOTE Confidence: 0.9392378

00:02:31.260 --> 00:02:32.960 cells, and so they extrinsically
NOTE Confidence: 0.9917061

00:02:33.260 --> 00:02:34.460 cause the death of those
NOTE Confidence: 0.9917061

00:02:34.460 --> 00:02:35.280 other cells.
NOTE Confidence: 0.97253704

00:02:35.820 --> 00:02:37.820 And it was learned that
NOTE Confidence: 0.97253704

00:02:37.820 --> 00:02:39.820 in addition to infected cells,
NOTE Confidence: 0.97253704

00:02:39.820 --> 00:02:41.055 T cells are also killing
NOTE Confidence: 0.97253704

00:02:41.215 --> 00:02:42.275 cancer cells recognizing
NOTE Confidence: 0.99932605

00:02:42.734 --> 00:02:43.715 cancer antigens
NOTE Confidence: 0.97126746

00:02:44.014 --> 00:02:45.075 that are expressed.
NOTE Confidence: 0.99750143

00:02:45.694 --> 00:02:46.194 But

NOTE Confidence: 0.9749638
00:02:46.495 --> 00:02:48.014 not every cancer has a
NOTE Confidence: 0.9749638
00:02:48.014 --> 00:02:49.375 good antigen and a t
NOTE Confidence: 0.9749638
00:02:49.375 --> 00:02:51.215 cell receptor that recognizes it
NOTE Confidence: 0.9749638
00:02:51.215 --> 00:02:52.174 in order to kill it.
NOTE Confidence: 0.9749638
00:02:52.174 --> 00:02:53.474 And so people have made
NOTE Confidence: 0.9749638
00:02:53.534 --> 00:02:55.294 what they call chimeric antigen
NOTE Confidence: 0.9749638
00:02:55.294 --> 00:02:55.794 receptors
NOTE Confidence: 0.9450393
00:02:56.174 --> 00:02:58.110 or CAR T cells, and
NOTE Confidence: 0.9450393
00:02:58.110 --> 00:03:00.510 the most successful example already
NOTE Confidence: 0.9450393
00:03:00.510 --> 00:03:02.430 approved is going after B
NOTE Confidence: 0.9450393
00:03:02.430 --> 00:03:04.210 cell leukemias and lymphomas
NOTE Confidence: 0.9129054
00:03:04.590 --> 00:03:06.350 against a molecule called CD
NOTE Confidence: 0.9129054
00:03:06.350 --> 00:03:06.850 nineteen.
NOTE Confidence: 0.9942904
00:03:08.270 --> 00:03:09.790 What we've been very interested
NOTE Confidence: 0.9942904
00:03:09.790 --> 00:03:11.565 in recently is expanding this
NOTE Confidence: 0.9942904

00:03:11.965 --> 00:03:13.185 to beyond
NOTE Confidence: 0.9790559

00:03:13.485 --> 00:03:15.805 these blood cancers to solid
NOTE Confidence: 0.9790559

00:03:15.805 --> 00:03:17.245 tumors. And so we've been
NOTE Confidence: 0.9790559

00:03:17.245 --> 00:03:19.085 going after other targets that
NOTE Confidence: 0.9790559

00:03:19.085 --> 00:03:19.825 are expressed
NOTE Confidence: 0.9900037

00:03:20.125 --> 00:03:21.885 highly on solid tumors and
NOTE Confidence: 0.9900037

00:03:21.885 --> 00:03:23.505 trying to boost the activity
NOTE Confidence: 0.9843361

00:03:23.885 --> 00:03:25.270 of these CAR T cells
NOTE Confidence: 0.9843361

00:03:25.270 --> 00:03:26.250 to kill them.
NOTE Confidence: 0.9746464

00:03:32.709 --> 00:03:34.230 The overall goal of the
NOTE Confidence: 0.9746464

00:03:34.230 --> 00:03:36.490 lab really is the selective
NOTE Confidence: 0.9592415

00:03:36.950 --> 00:03:38.805 therapeutic control of cell death.
NOTE Confidence: 0.99481106

00:03:39.765 --> 00:03:41.224 I'm a physician scientist.
NOTE Confidence: 0.9915751

00:03:41.844 --> 00:03:43.444 I spend eighty percent of
NOTE Confidence: 0.9915751

00:03:43.444 --> 00:03:45.204 my time running this research
NOTE Confidence: 0.9915751

00:03:45.204 --> 00:03:46.805 laboratory. The other twenty percent

NOTE Confidence: 0.9915751
00:03:46.805 --> 00:03:48.004 of my time, I'm a
NOTE Confidence: 0.9915751
00:03:48.004 --> 00:03:48.504 hematopathologist
NOTE Confidence: 0.79614544
00:03:49.284 --> 00:03:50.344 where I'm diagnosing,
NOTE Confidence: 0.9994783
00:03:51.204 --> 00:03:51.704 lymphomas,
NOTE Confidence: 0.95596087
00:03:52.084 --> 00:03:52.584 leukemias,
NOTE Confidence: 0.99949837
00:03:53.090 --> 00:03:53.910 and myelomas
NOTE Confidence: 0.95736635
00:03:54.210 --> 00:03:55.110 within patients.
NOTE Confidence: 0.98792255
00:03:55.410 --> 00:03:57.490 And so I'm very familiar
NOTE Confidence: 0.98792255
00:03:57.490 --> 00:03:59.170 with the blood system and
NOTE Confidence: 0.98792255
00:03:59.170 --> 00:04:00.290 how it can produce cancers,
NOTE Confidence: 0.98792255
00:04:00.290 --> 00:04:01.250 but I'm also very familiar
NOTE Confidence: 0.98792255
00:04:01.250 --> 00:04:02.050 with the blood system and
NOTE Confidence: 0.98792255
00:04:02.050 --> 00:04:03.270 how it can be harnessed
NOTE Confidence: 0.98792255
00:04:03.410 --> 00:04:04.450 in order to,
NOTE Confidence: 0.79095125
00:04:04.770 --> 00:04:05.270 affect,
NOTE Confidence: 0.98815084

00:04:05.730 --> 00:04:06.230 cure.