

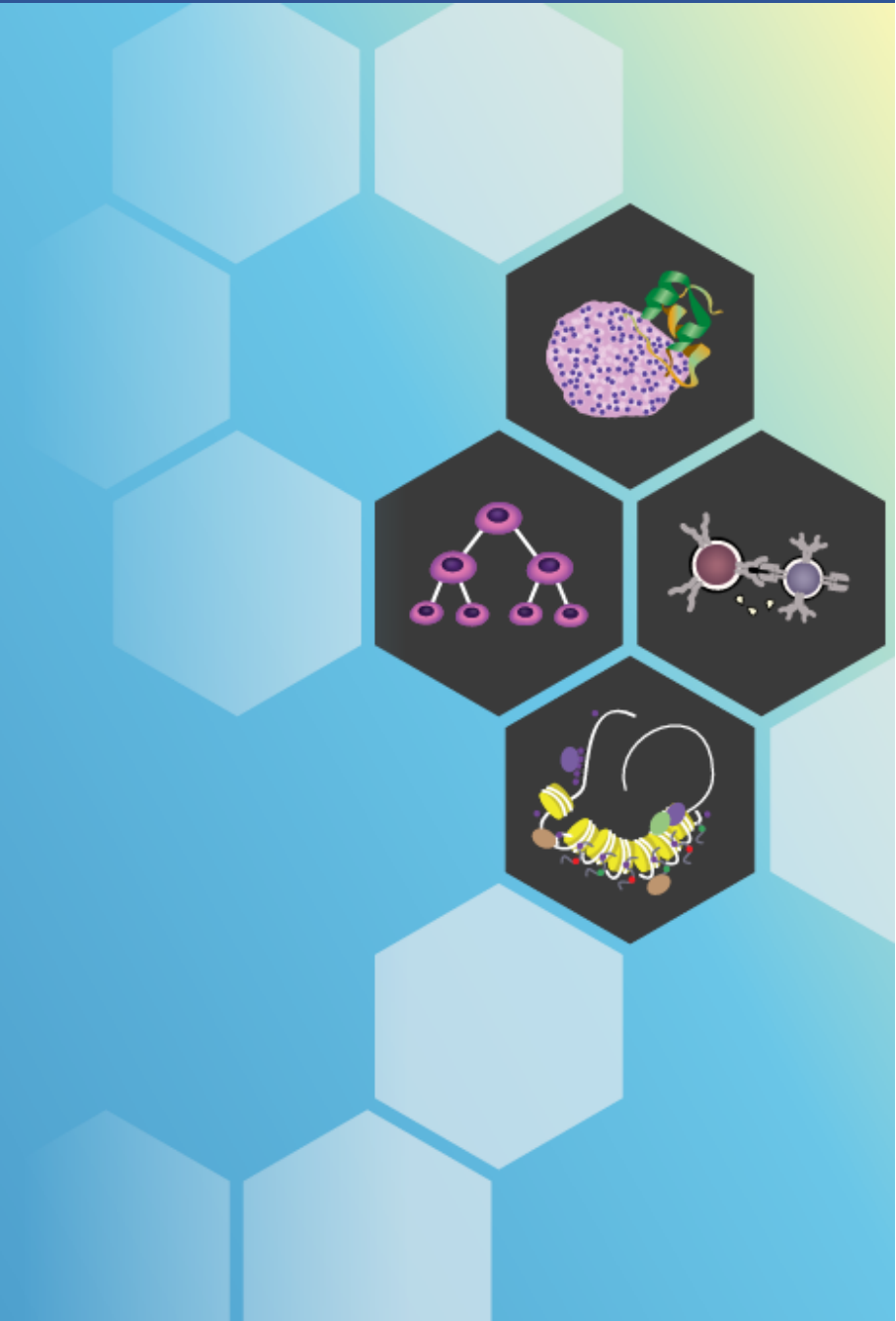
2024 RACHMIEL LEVINE-ARTHUR RIGGS

Diabetes Research Symposium

Early Onset Colon Cancer and Obesity

Emina Huang, MD, MBA

UT Southwestern Medical Center



Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

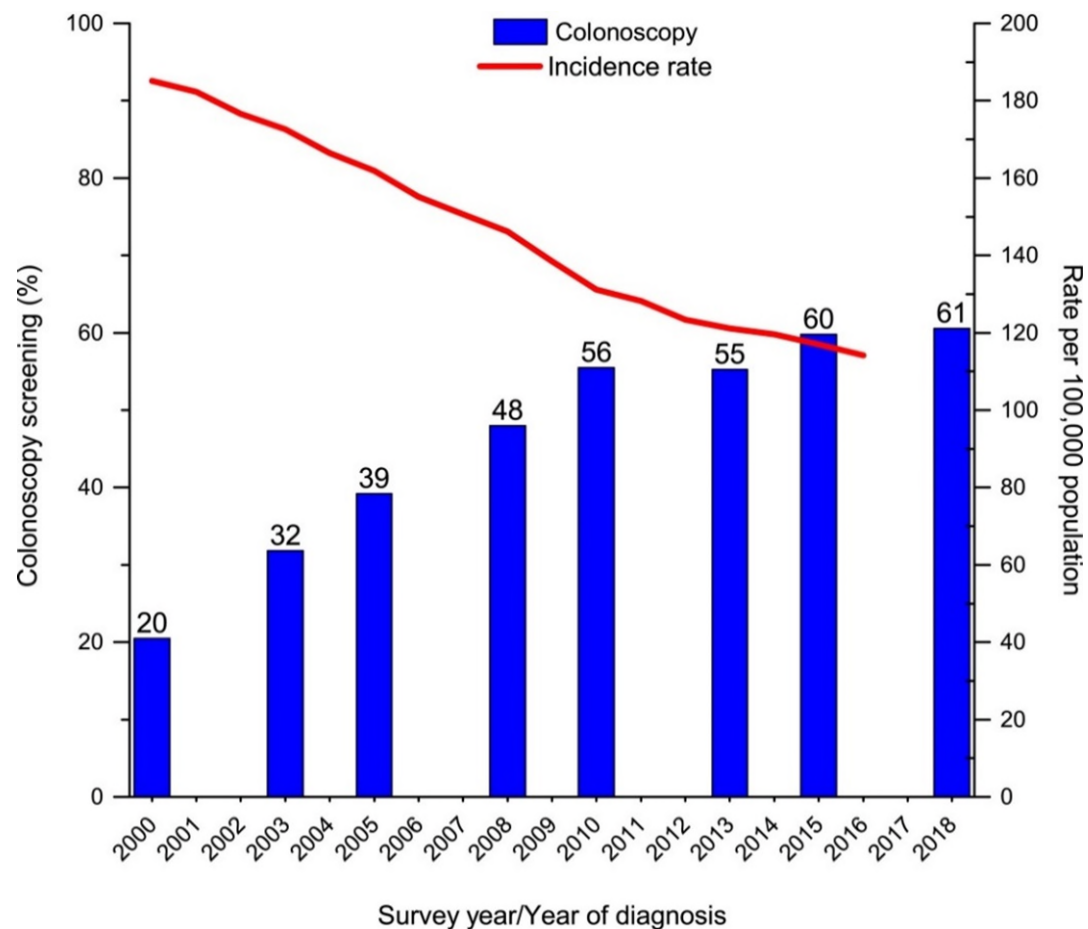
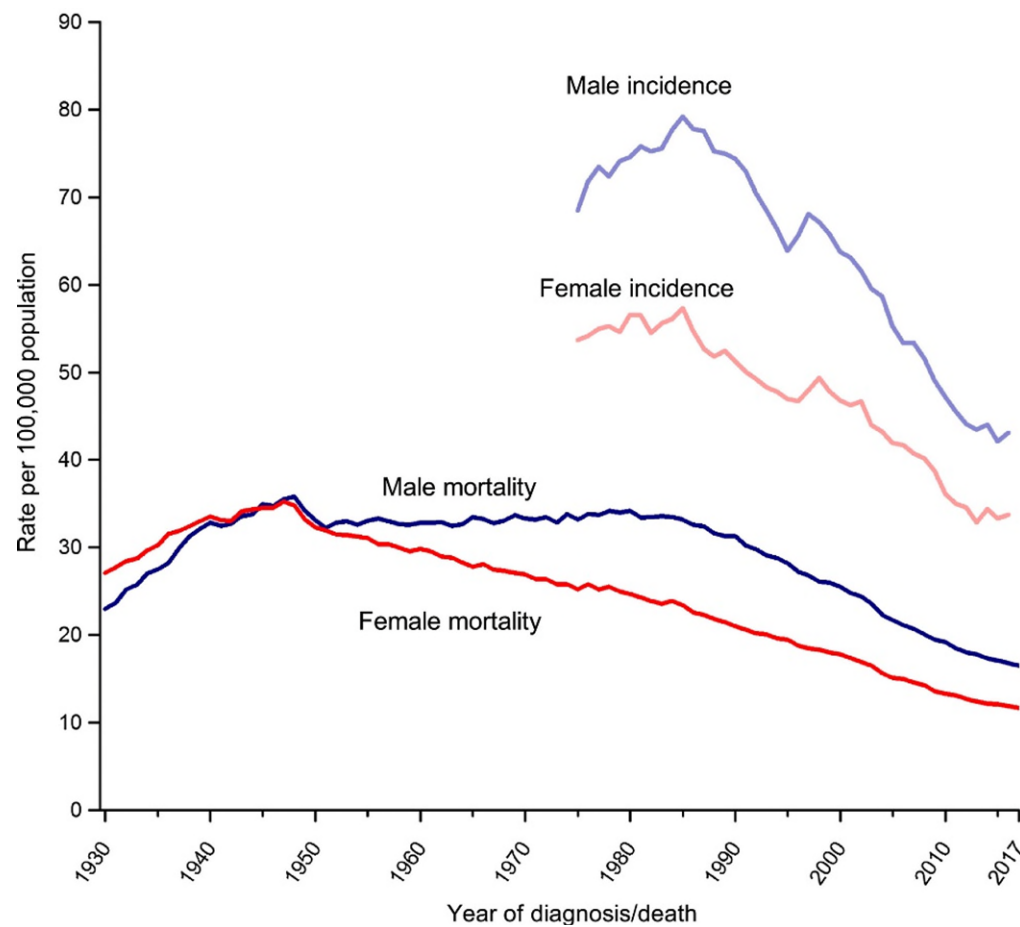
The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

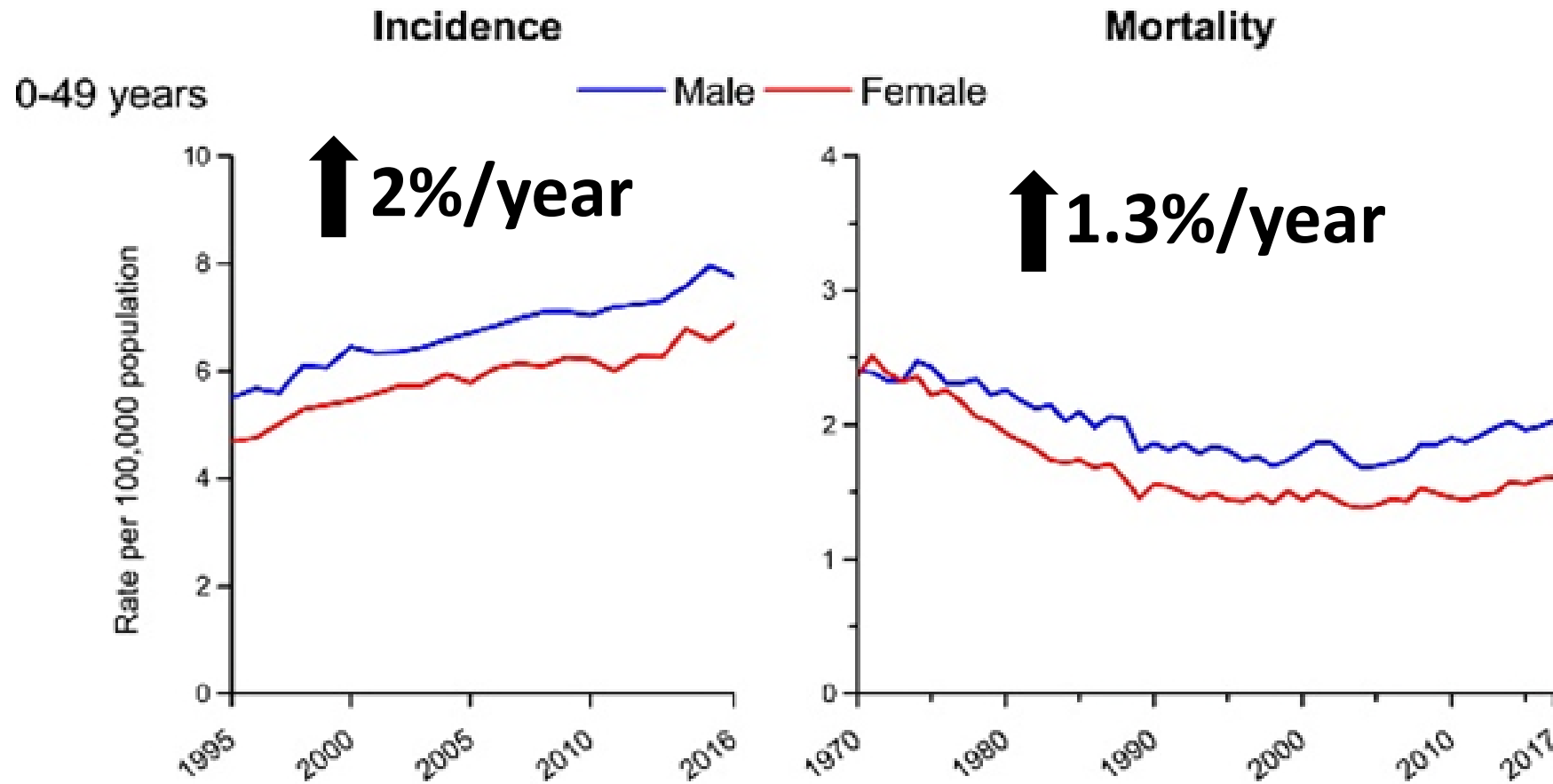
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Colorectal Cancer Is Decreasing Overall



But Rates Are Rising in Those Under 50



- In those under 50, #1 cancer cause of death in men, #3 in women
- Deaths are increasing in those under 50, even though deaths are decreasing by 3%/year in those over 65.

Local and National Increases in Early Onset Colorectal Cancer

- Currently, early onset disease accounts for 11% of colon cancers and 18% of rectal cancers.
- In Dallas County, 12.9% of colorectal cancers were early onset in 2017.
- At UTSW, 31.4% of colorectal cancers discussed at multidisciplinary tumor board meetings since January 2021 have been early onset cases.
- Increases in early onset cases expected by 2030:
 - Colon cancer: ↑2x
 - Rectal cancer: ↑4x

What May Influence Colorectal Cancer Development?

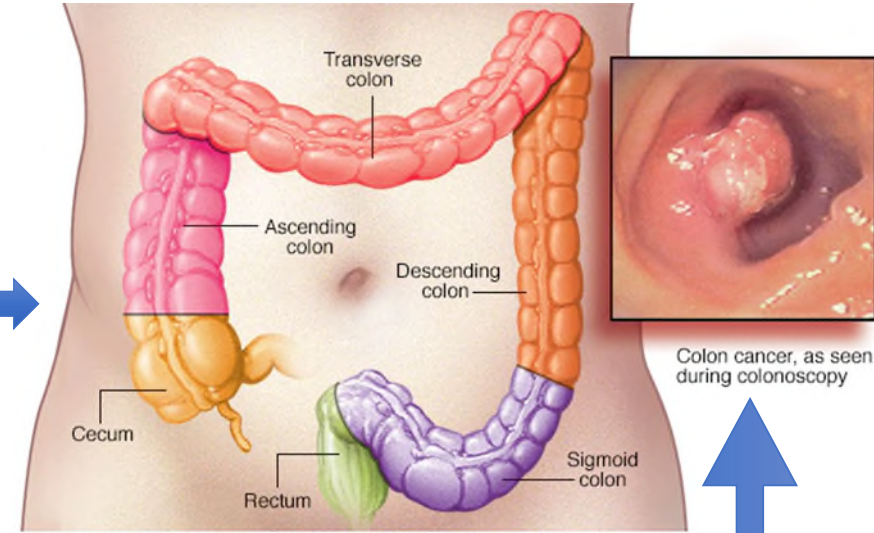
Early-life exposures

- Maternal nutrition, infection, medications, stress
- Method of feeding
- Frequency of antibiotic use

Environmental factors

- Red and processed meats
- **Western diet**
- **Sedentary lifestyle**
- Water quality
- Environmental quality near home

Microbiome development



© MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

- Immunity
- **Inflammation**
- **Obesity**
- Diabetes

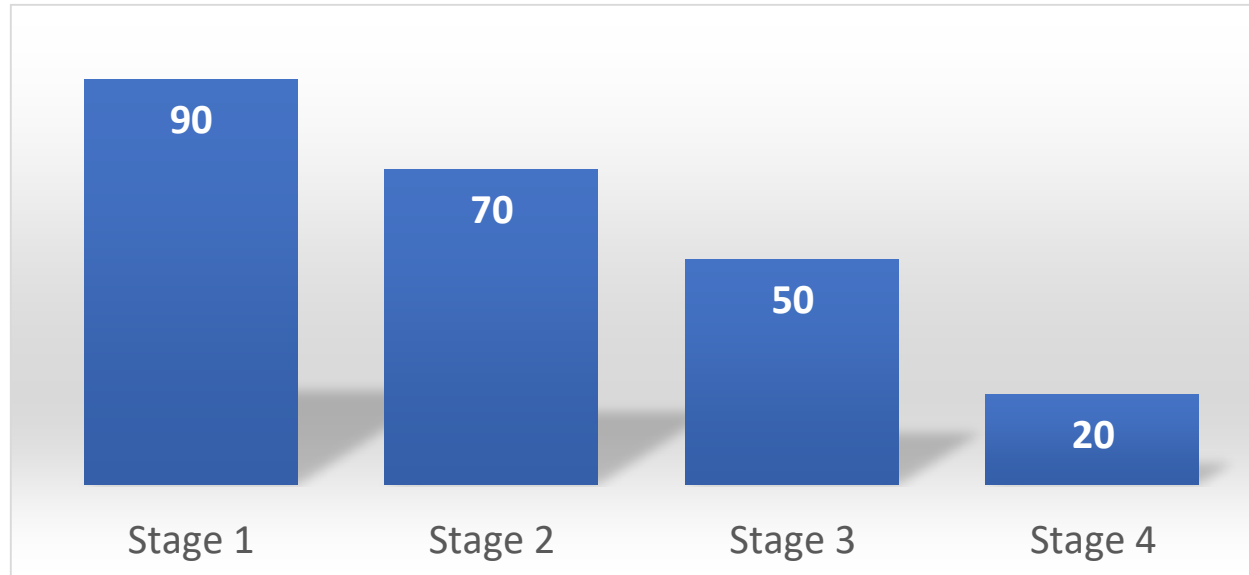
Infancy

Childhood

Adulthood

Catching Cancer Early Is Key

Colorectal Cancer 5-Year Survival Percentages Based on Stage at Diagnosis

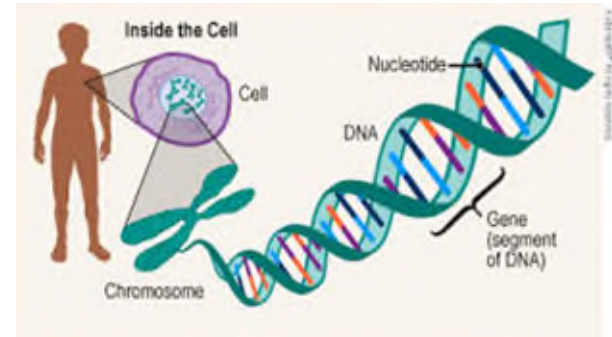


Screening for colorectal cancer should

BEGIN AT 45

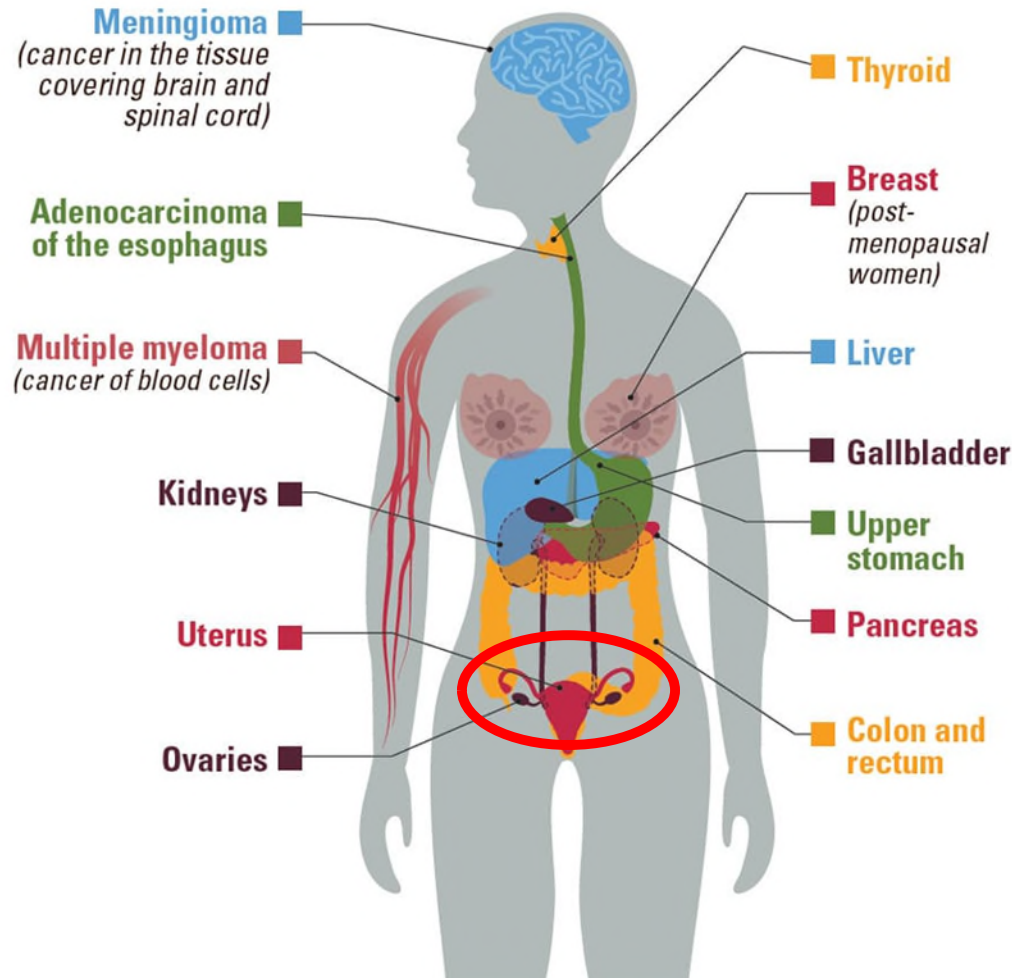
Special Considerations for Early Onset Patients

- Treatments can be stronger both before and after surgery
- Early onset of disease has broad implications for these patients' lives:



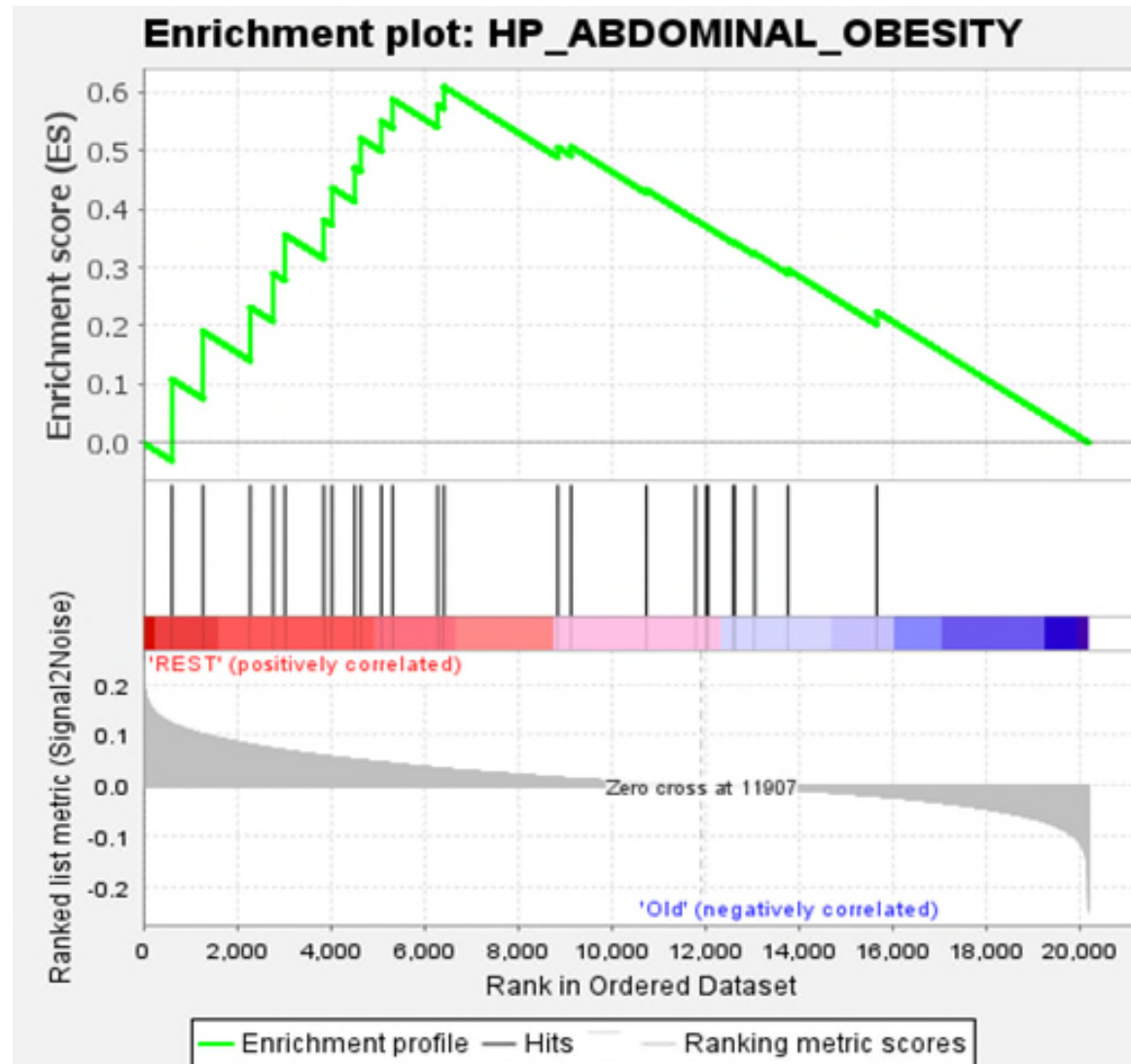
Obesity (minimally) Promotes CRC

13 cancers are associated with overweight and obesity

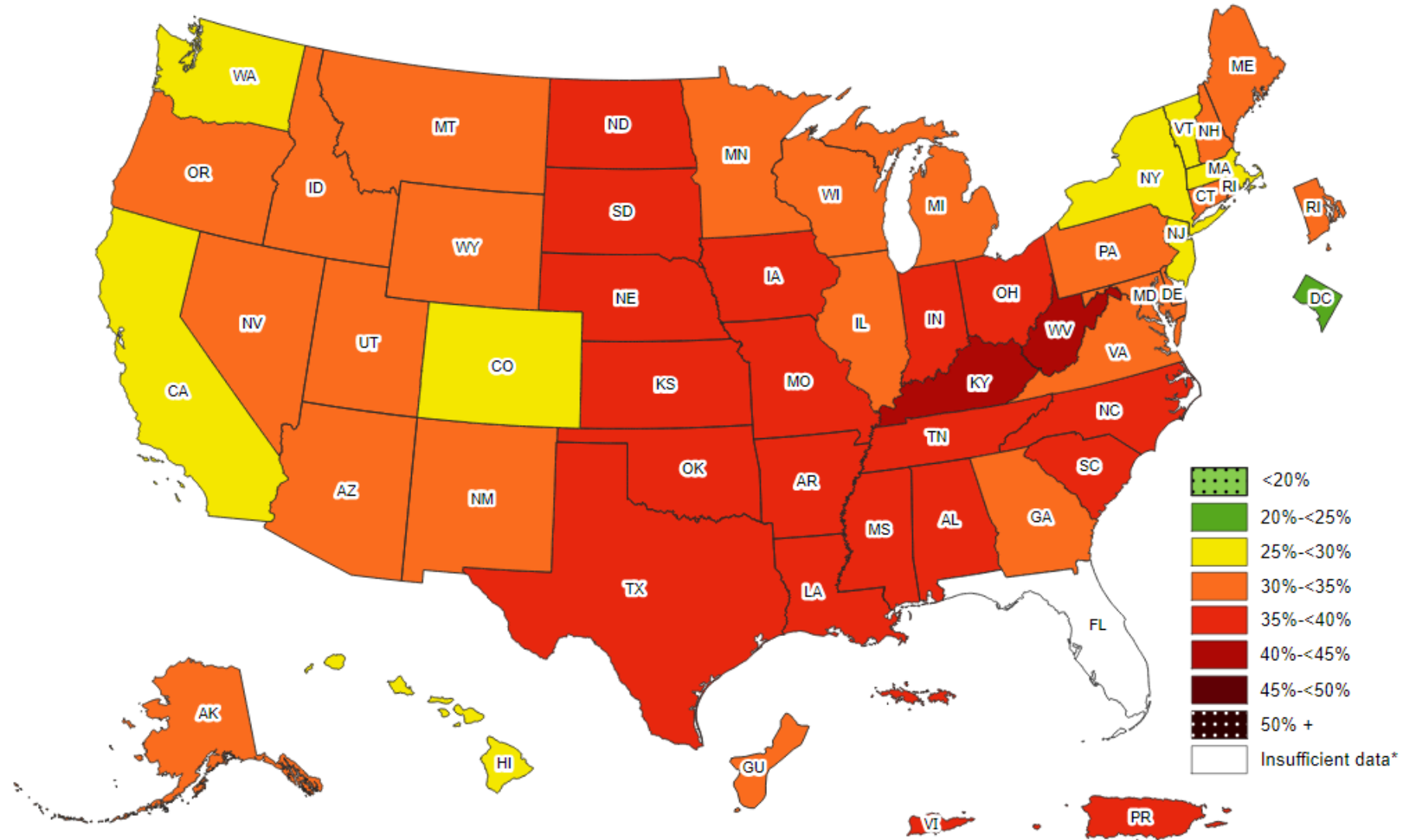


Cancer type (reference)	Compared with people without obesity or overweight, this cancer is
Endometrial (9, 10)	7 times as likely in people with severe obesity* 2-4 times as likely in people with obesity or overweight
Esophageal adenocarcinoma (11)	4.8 times as likely in people with severe obesity 2.4-2.7 times as likely in people with obesity 1.5 times as likely in people with overweight
Gastric cardia (12)	2 times as likely in people with obesity
Liver (13, 14)	2 times as likely in people with obesity or overweight
Kidney (15, 16)	2 times as likely in people with obesity or overweight
Multiple myeloma (17)	1.1-1.2 times as likely in people with obesity or overweight
Meningioma (18)	1.5 times as likely in people with obesity 1.2 times as likely in people with overweight
Pancreatic (19)	1.5 times as likely in people with obesity or overweight
Colorectal (20)	1.3 times as likely in people with obesity
Gallbladder (21, 22)	1.6 times as likely in people with obesity 1.2 times as likely in people with overweight
Breast Postmenopausal (23, 24)	1.2-1.4 times as likely in people with obesity or overweight 1.2 times as likely for every 5-unit increase in BMI
Premenopausal** (24, 25)	0.8 times as likely in people with obesity or overweight
Ovarian*** (26, 27)	1.1 times as likely for every 5-unit increase in BMI
Thyroid (28)	1.3 times as likely in people with obesity 1.26 times as likely in people with overweight

Obesity promotes CRC ... in EO CRC

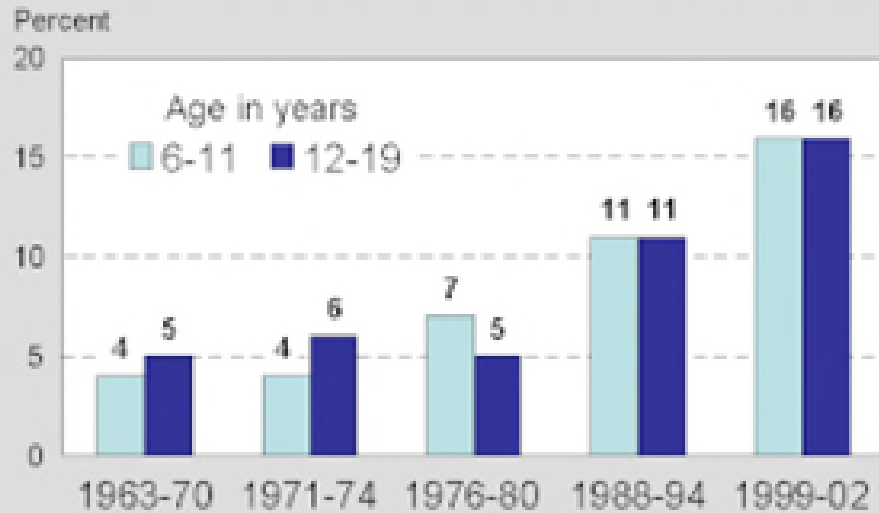


National Obesity Rates



The increase in childhood obesity may contribute

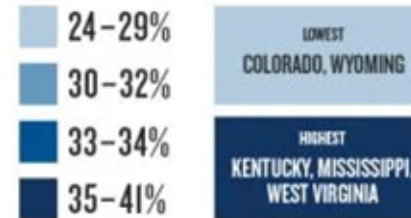
Figure 1. Prevalence of overweight among children and adolescents ages 6-19 years



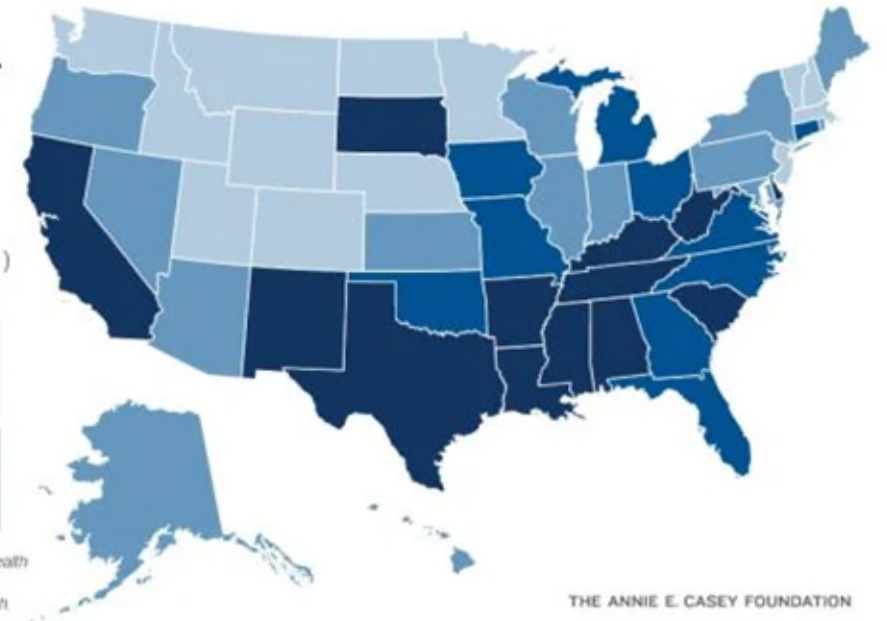
NOTE: Excludes pregnant women starting with 1971-74. Pregnancy status not available for 1963-65 and 1966-70. Data for 1963-65 are for children 6-11 years of age; data for 1966-70 are for adolescents 12-17 years of age, not 12-19 years.
SOURCE: CDC/NCHS, NHES and NHANES

Nationally, 1 in 3 Children Are Overweight or Obese. Highest Rates Found in the South.

Percentage of Children and Teens Who Are Overweight or Obese (2020-21)

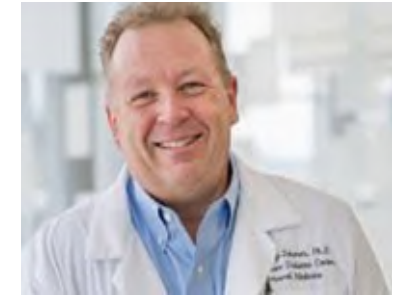
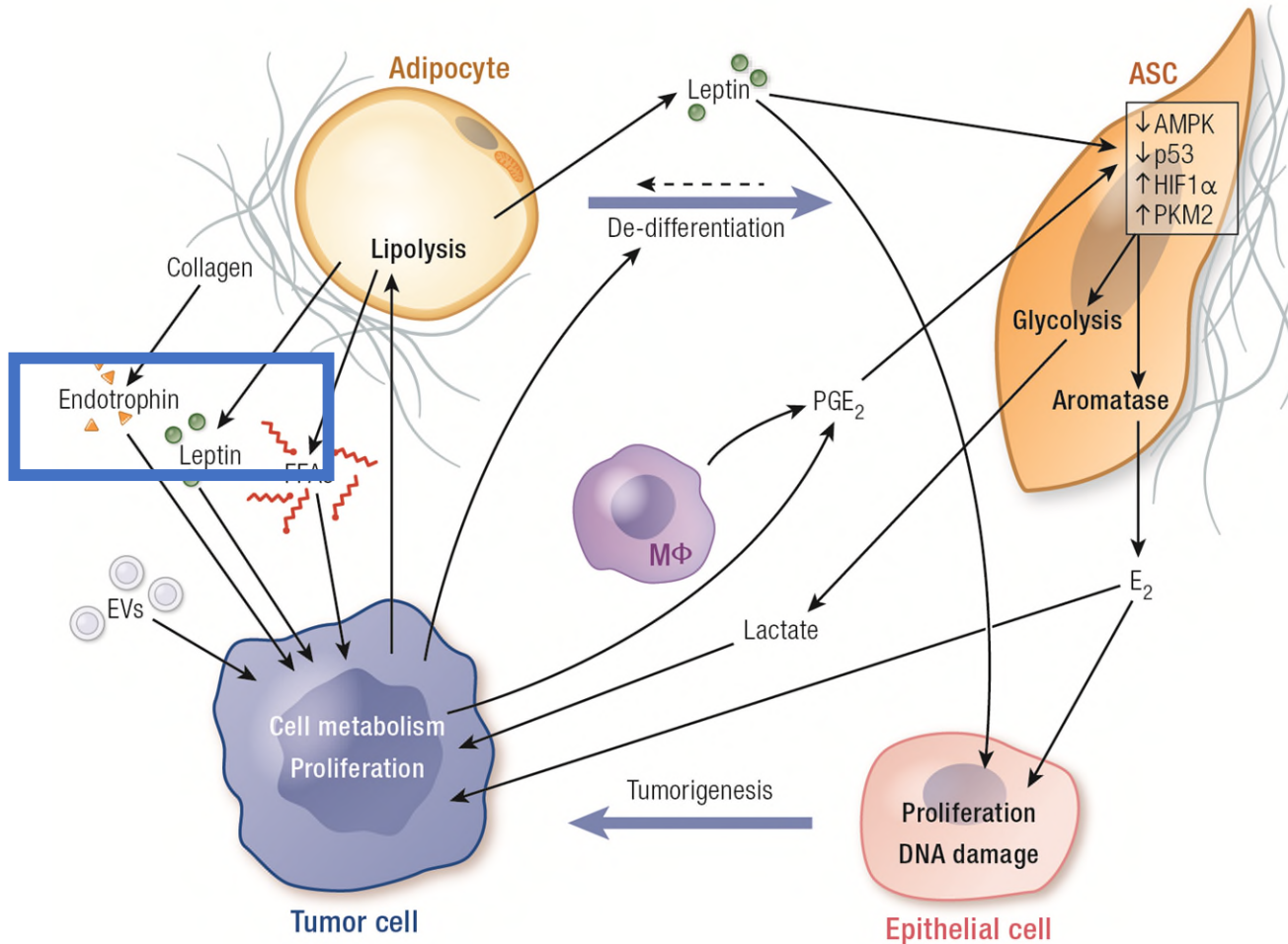


Source: U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Bureau, 2020-21 National Survey of Children's Health

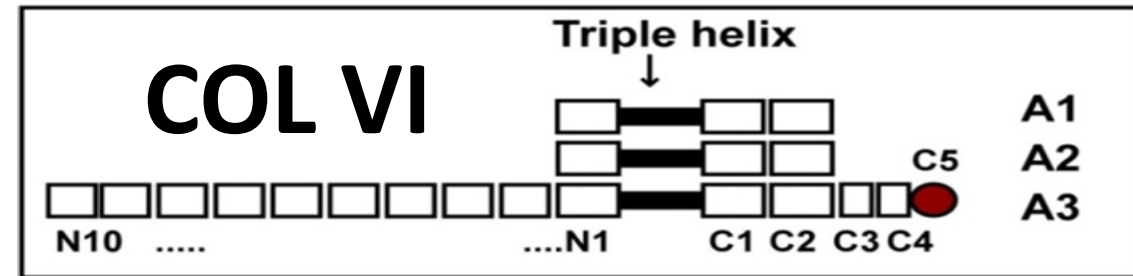


THE ANNIE E. CASEY FOUNDATION

We needed a wedge ...



Philipp Scherer, PhD



Endotrophin, roles in fibroinflammatory diseases

- Liver diseases

- Steatohepatitis: Hagstrom and Scherer, Scandinavian Journal of Gastroenterology

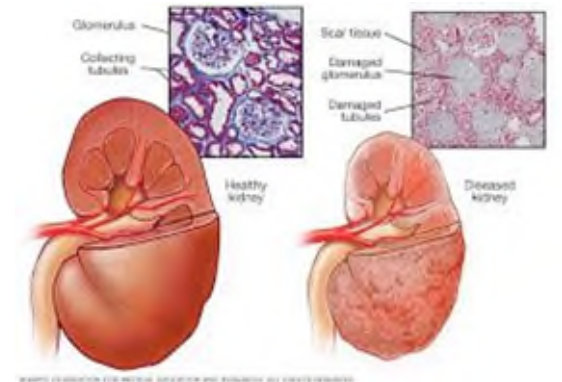
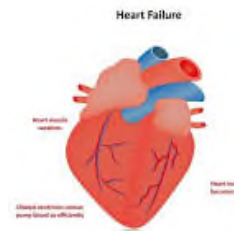


- Renal disease

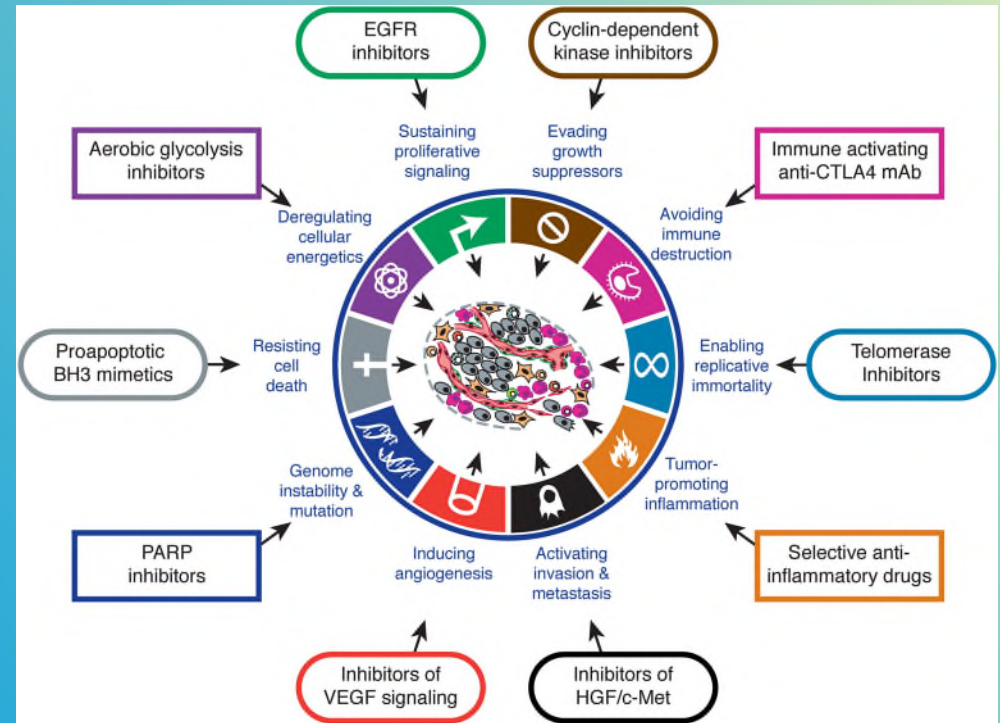
- AKI and mortality: Sparding N, Kidney360, 2022
- ESRD: Javier Neyra, Orson Moe. Kidney360. 2024 Jul 18. doi: 10.34067/KID.0000000000000507.
- Lupus nephritis, IgA nephropathy: Genovese F, Karsdal MA, Kidney 360, 2021

- Cardiac disease: Heart Failure

- Lee PC, Scherer P. iScience, July 2024
- Chirinos JA, Cappola TP, NEJM Evidence, 2022

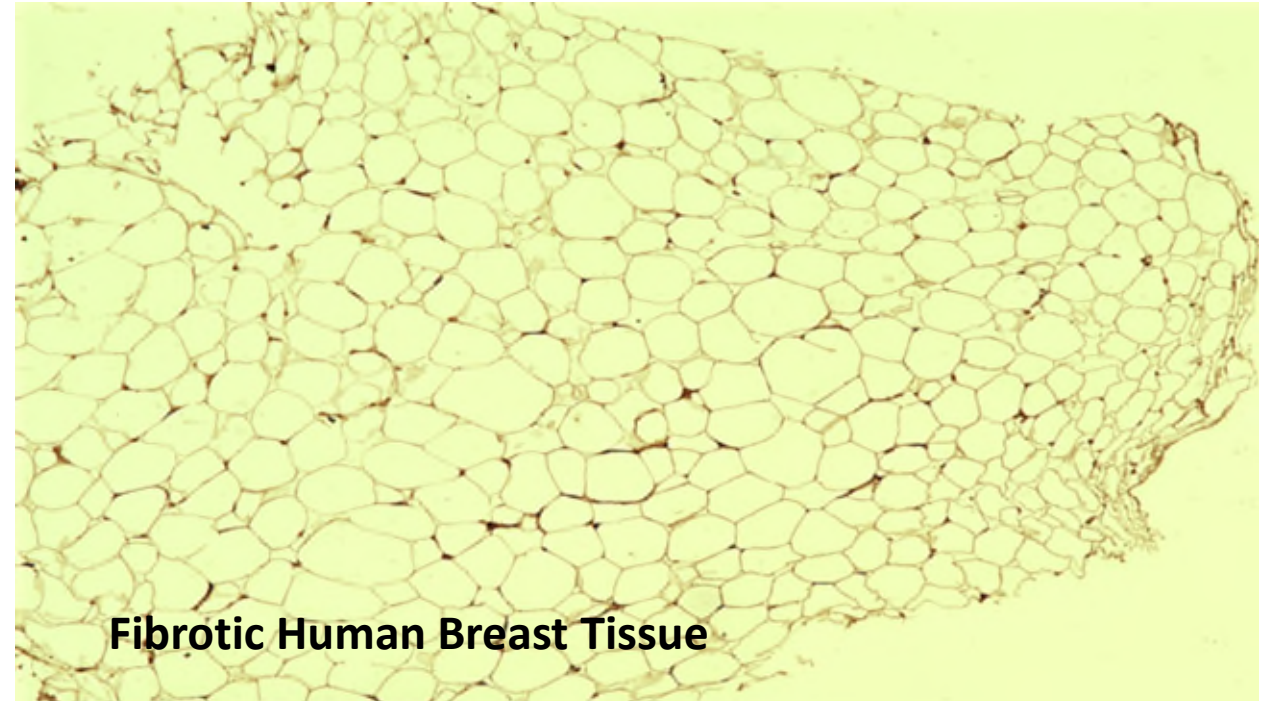


Is there a role in cancer?

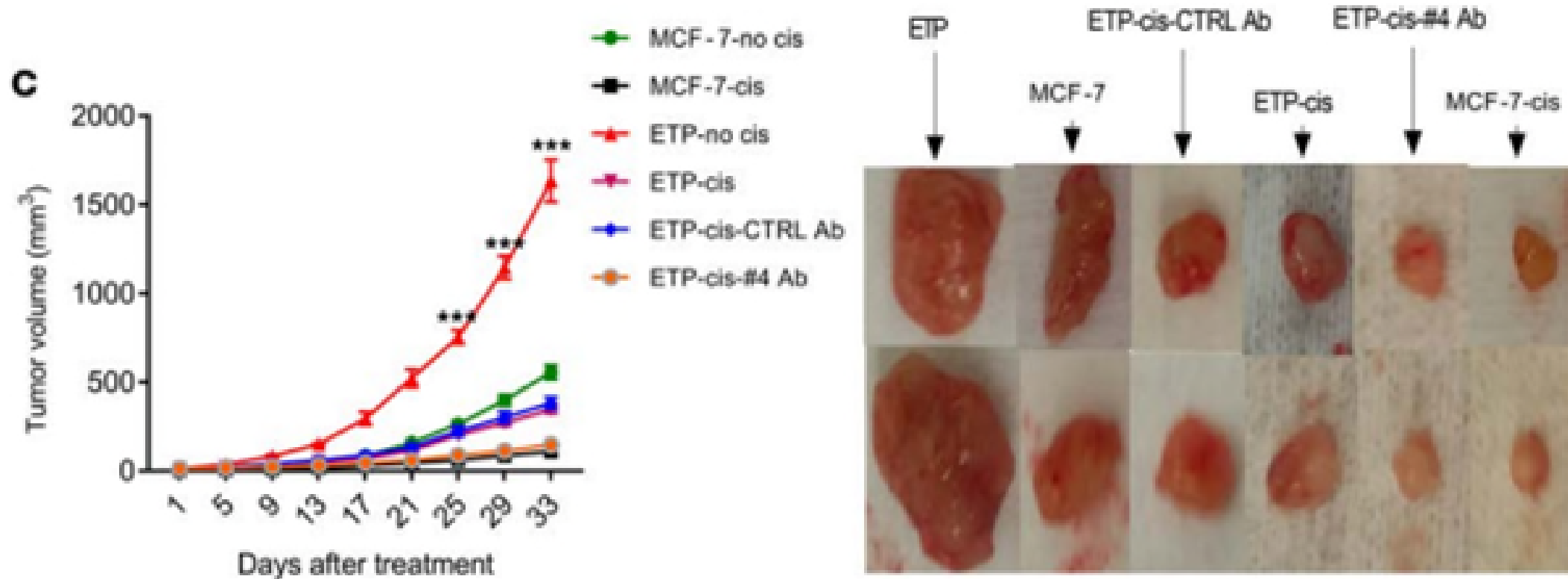


Hanahan D, Weinberg R, Cell 2011

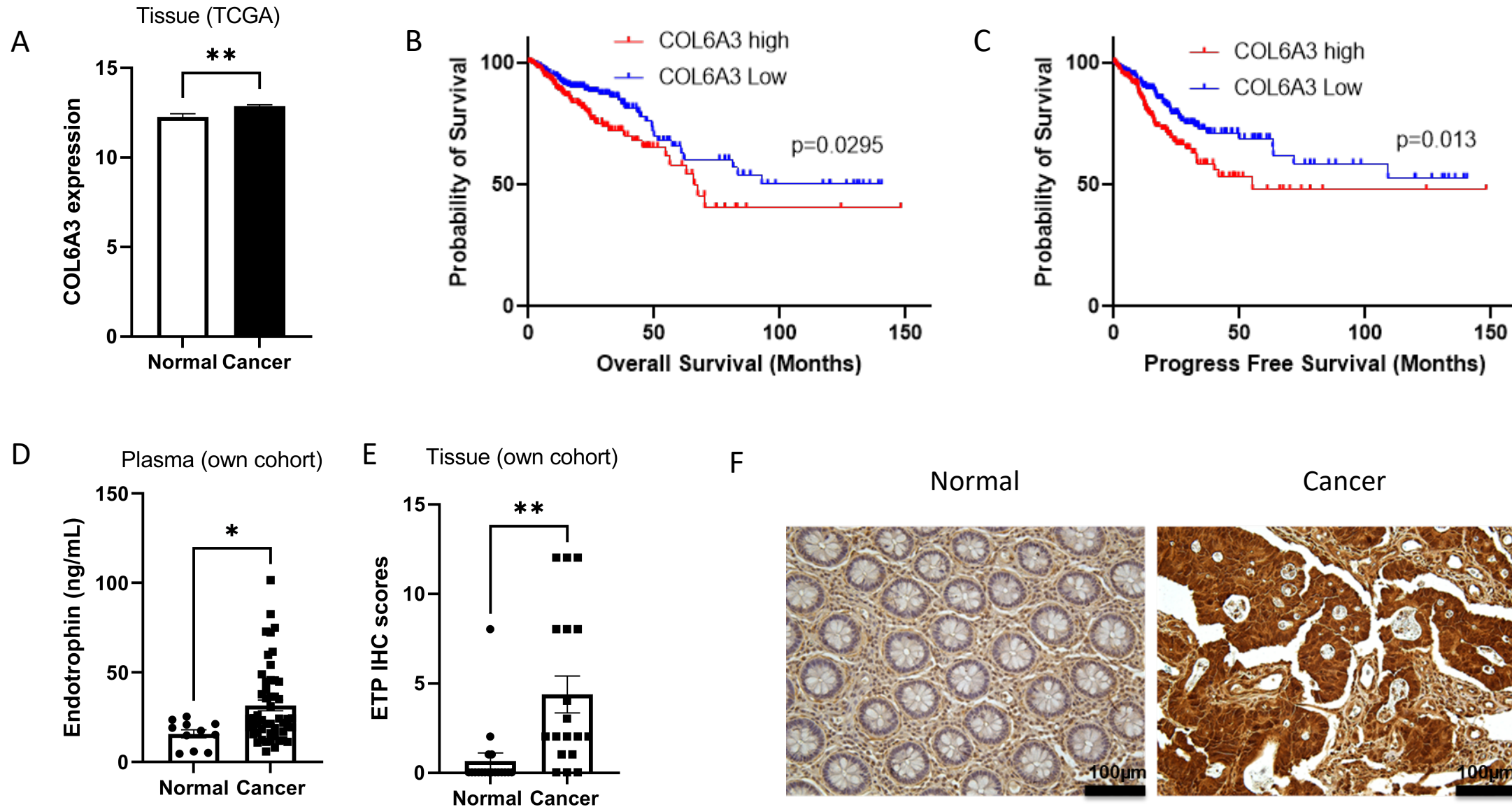
What about Breast Cancer ...



Anti-ETP augments cisplatin efficacy *in vivo*

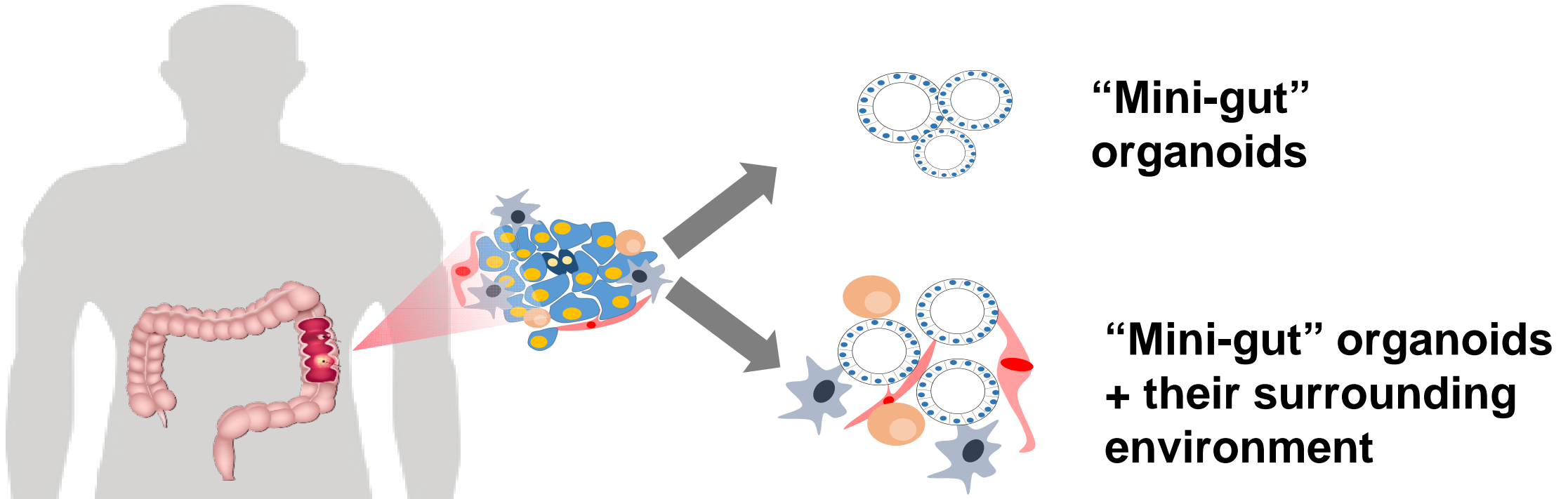


Elevated COL6A3 and ETP levels predict poorer survival



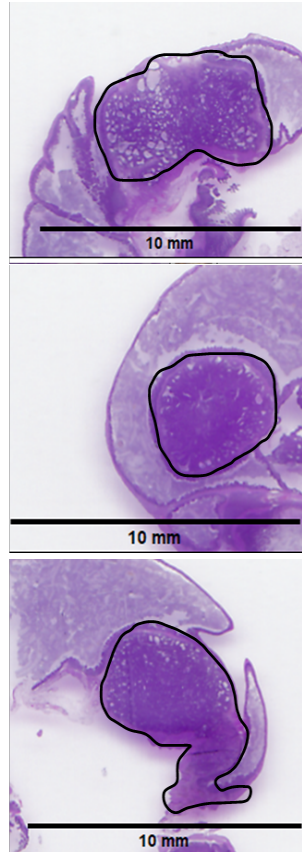
Unpublished data

Growing organoids ...

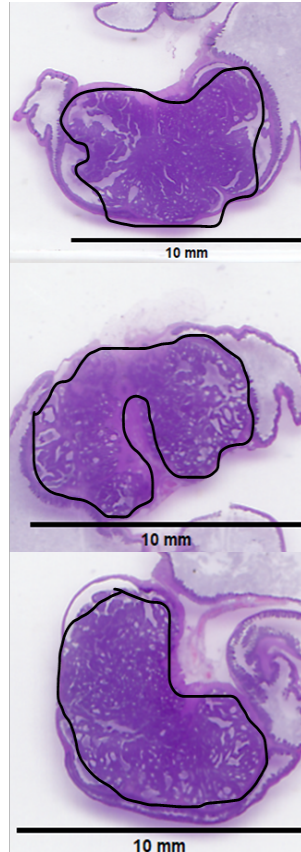


Orthotopic Placement

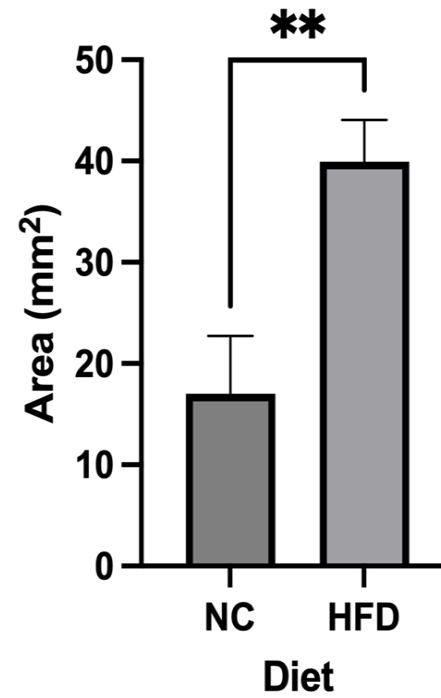
A Normal Chow



High Fat Diet



B



Visceral Fat in NSG mice fed a High-fat Diet

A

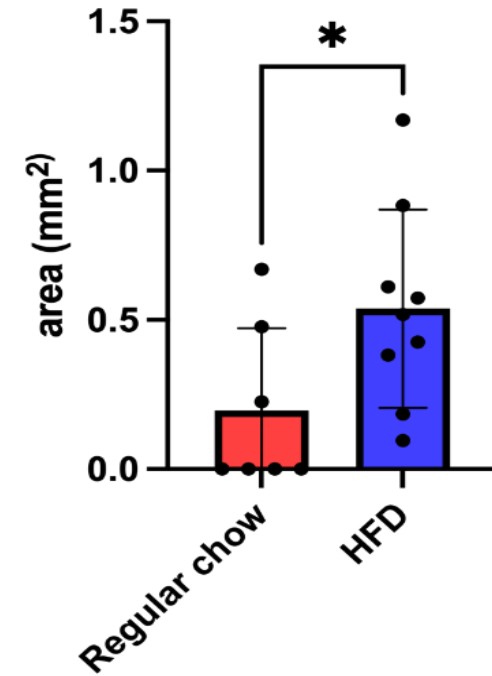


Regular Diet



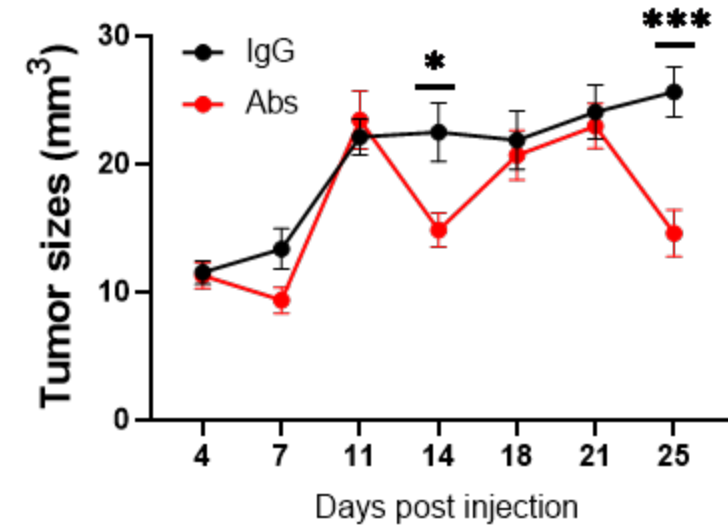
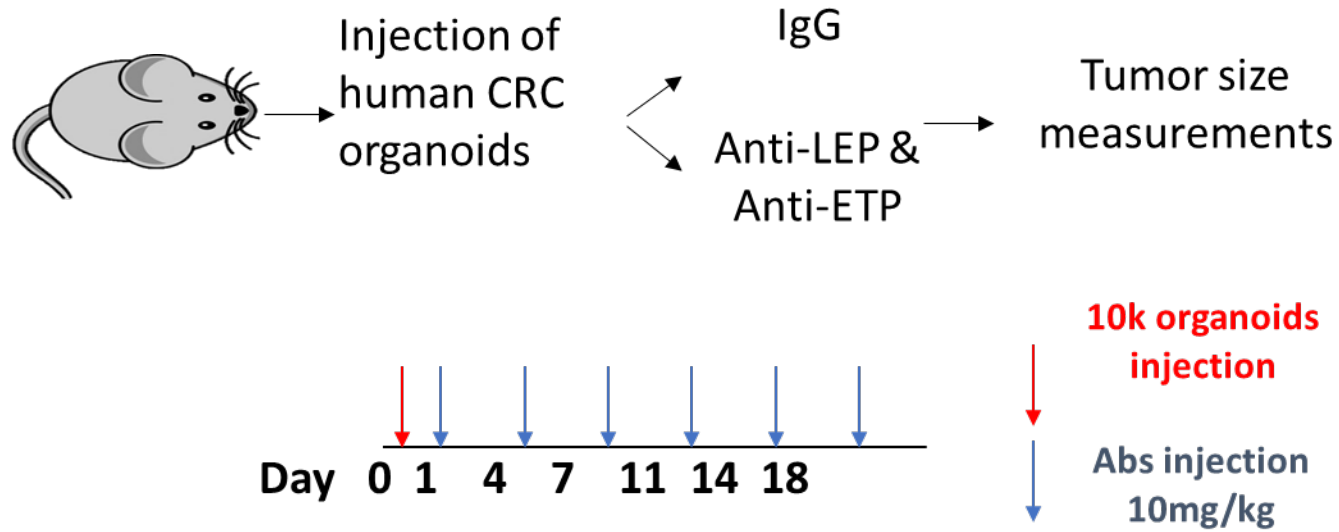
High Fat Diet

B



Unpublished data

More Data



Future plans ...

- What is the receptor?
- Can we mitigate orthotopic growth?
- Can we mitigate growth due to the strongest driver genes?
- What about the immune system?
- Can anti-ETP be used adjuvantly?

Questions?

