

OCCPI
Ohio Colorectal Cancer Prevention Initiative

The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Happy Lynch Syndrome Awareness Day March 22, 2016

Thanks to the Lynch Syndrome Screening Network (LSSN) for sponsoring this webinar

www.lynchscreening.net

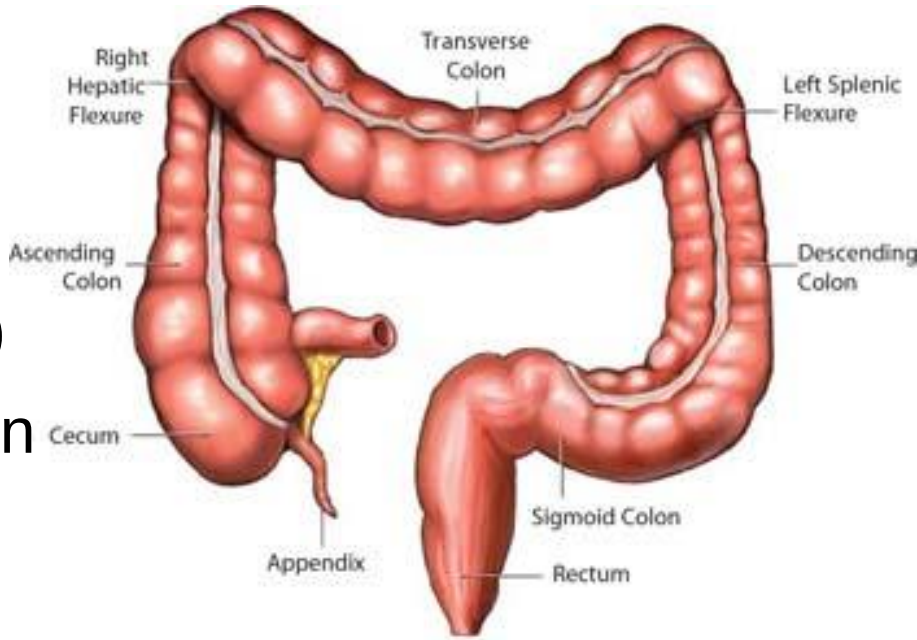
The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER



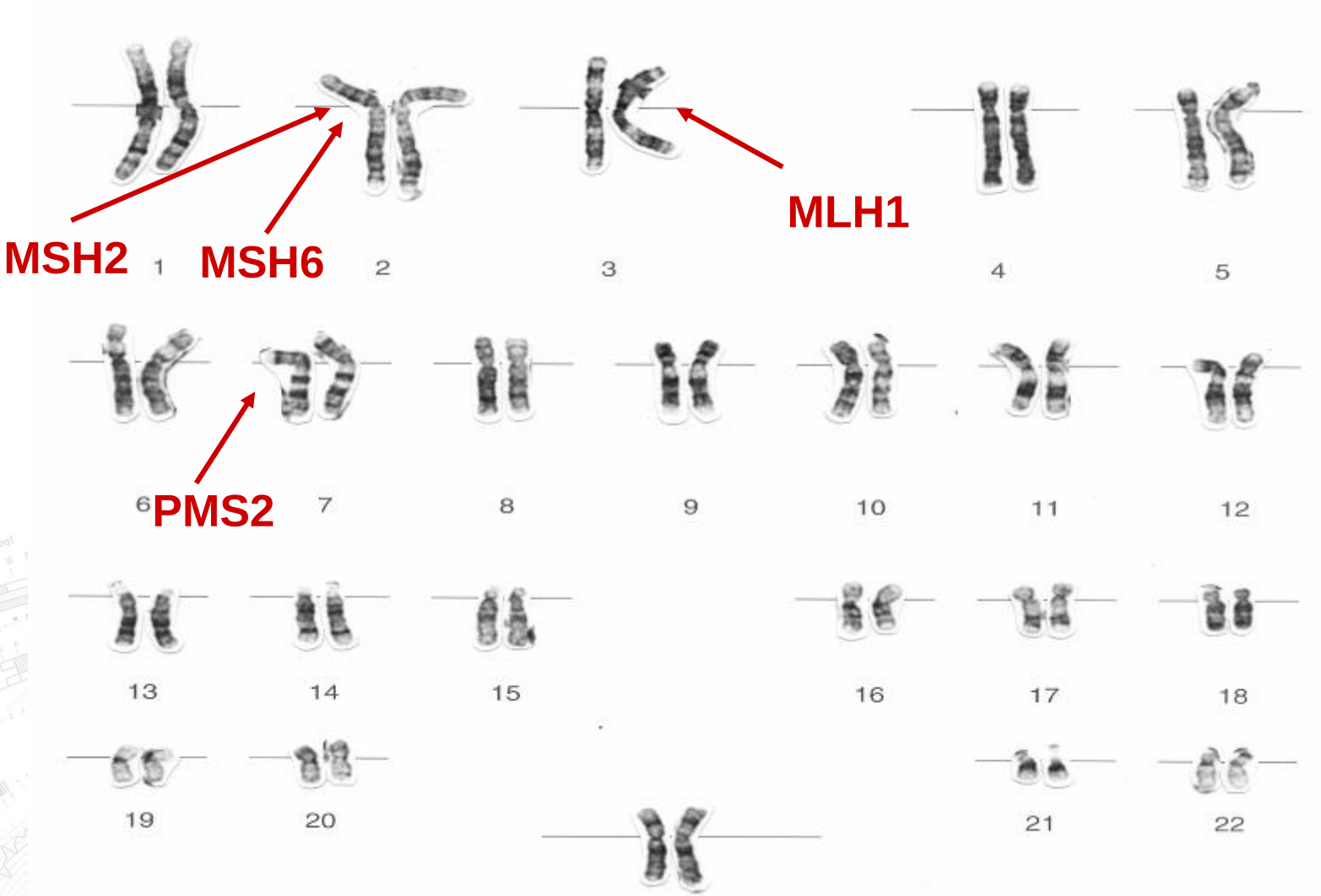
Lynch Syndrome

- The most common cause of inherited colorectal (CRC) and endometrial (EC) cancers
- Early but variable age at CRC diagnosis (~45 years)
- Tumor site in proximal colon predominates
- Extracolonic cancers: endometrium, ovary, stomach, urinary tract, small bowel, bile ducts, sebaceous skin tumors

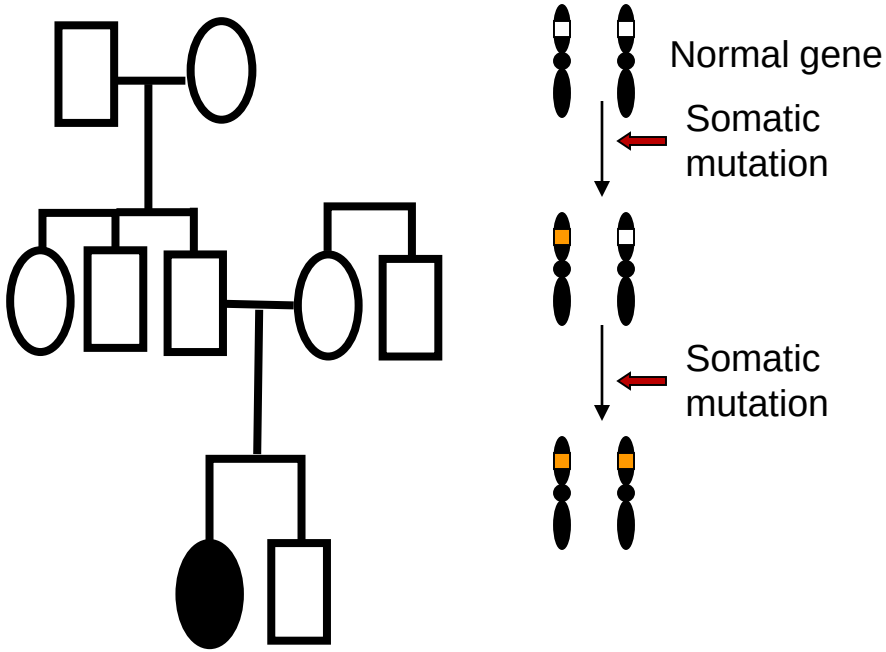


Anatomy of Large Intestine

Lynch Syndrome

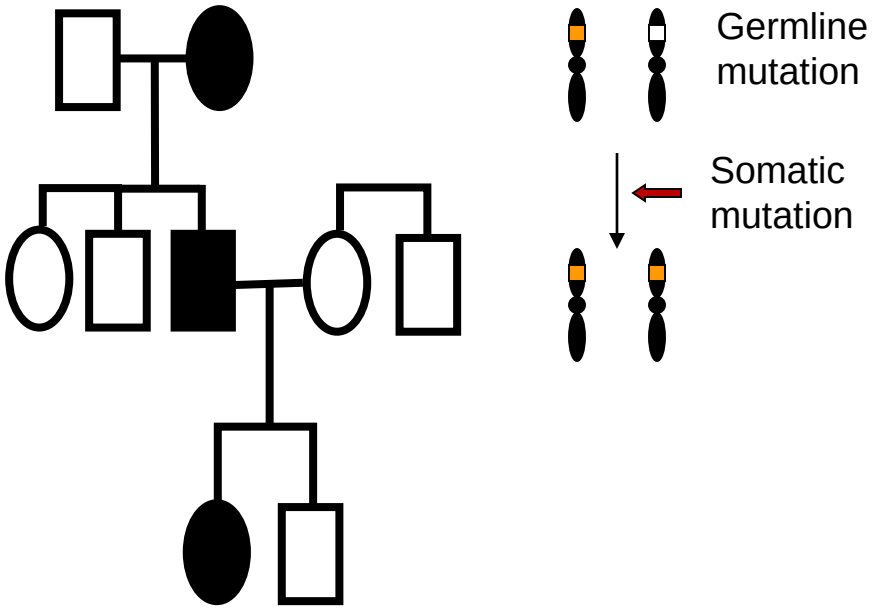


Sporadic



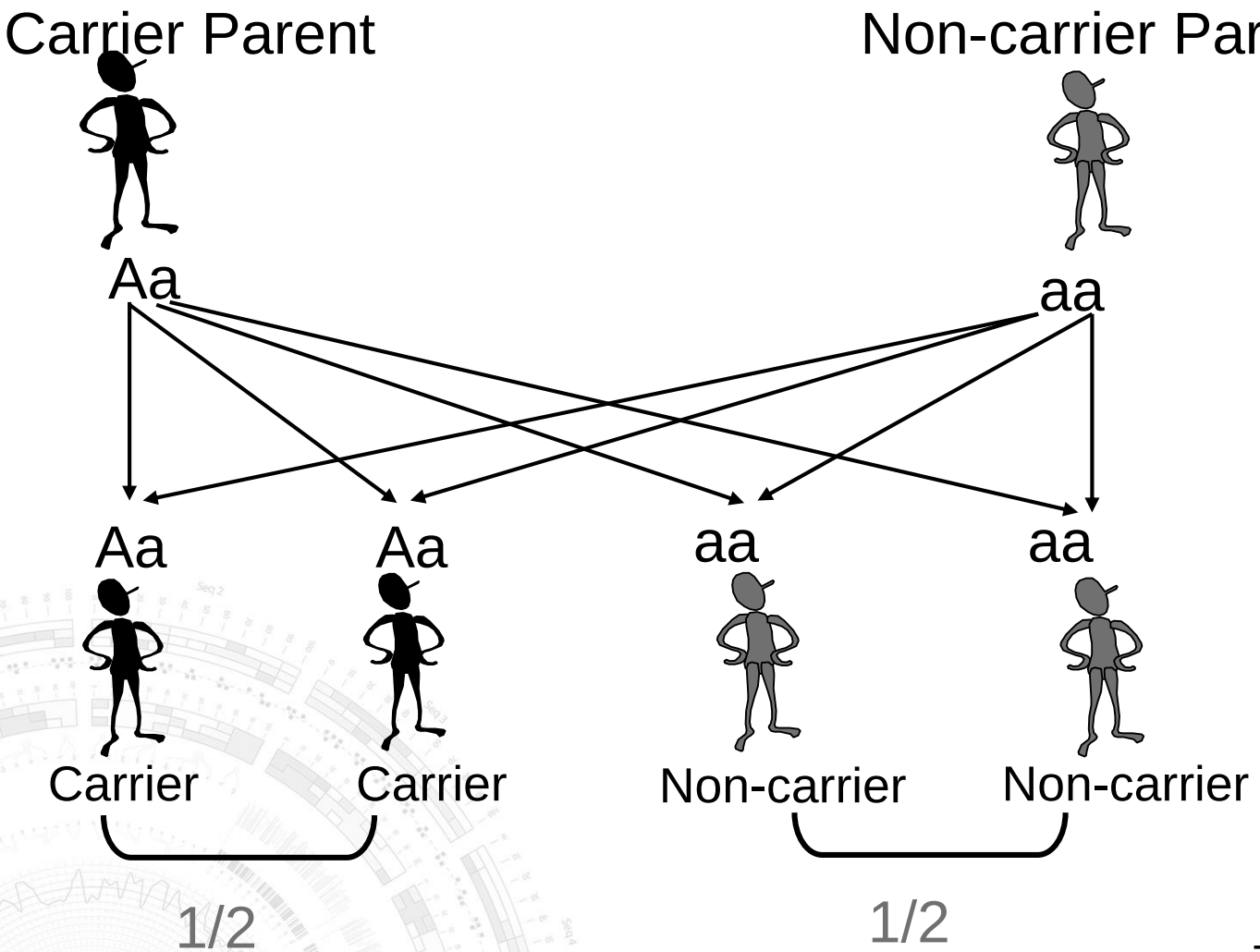
- Later age at onset (60s or 70s)
- Little or no family history of cancer
- Single or unilateral tumors

Inherited



- Early age at onset (<50)
- Multiple generations with cancer
- Clustering of certain cancers (i.e. breast/ovarian)

Autosomal Dominant Inheritance



Th

Lynch Syndrome Cancer Risks (to 70)

Cancer type	MLH1& MSH2	MSH6	PMS2	General Public
Colon cancer	40-80%	10-22%	15-20%	5.5%
Endometrial cancer	25-60%	16-26%	15%	2.7%
Stomach	1-13%	≤ 3%	6%	<1%
Ovarian	4-24%	1-11%	6%	1.6%

NCCN Guidelines for Colorectal Cancer Screening 2.2014; Bonadona V. JAMA 2011;30-5:2304-10.; Senter L. Gastroenterology

Lynch syndrome Surveillance Options

Intervention	Recommendation
Colonoscopy	Every 1-2 y beginning at: Age 20-25 (MLH1 & MSH2), or Age 25-30 (MSH6 & PMS2)
Endometrial sampling	Every 1 y beginning at age 30-35
Transvaginal U/S	Every 1 y beginning at age 30-35
Urinalysis with cytology	Every 1-2 y beginning at age 25-35
History & Exam w/ review of systems	Every 1 y beginning at age 21

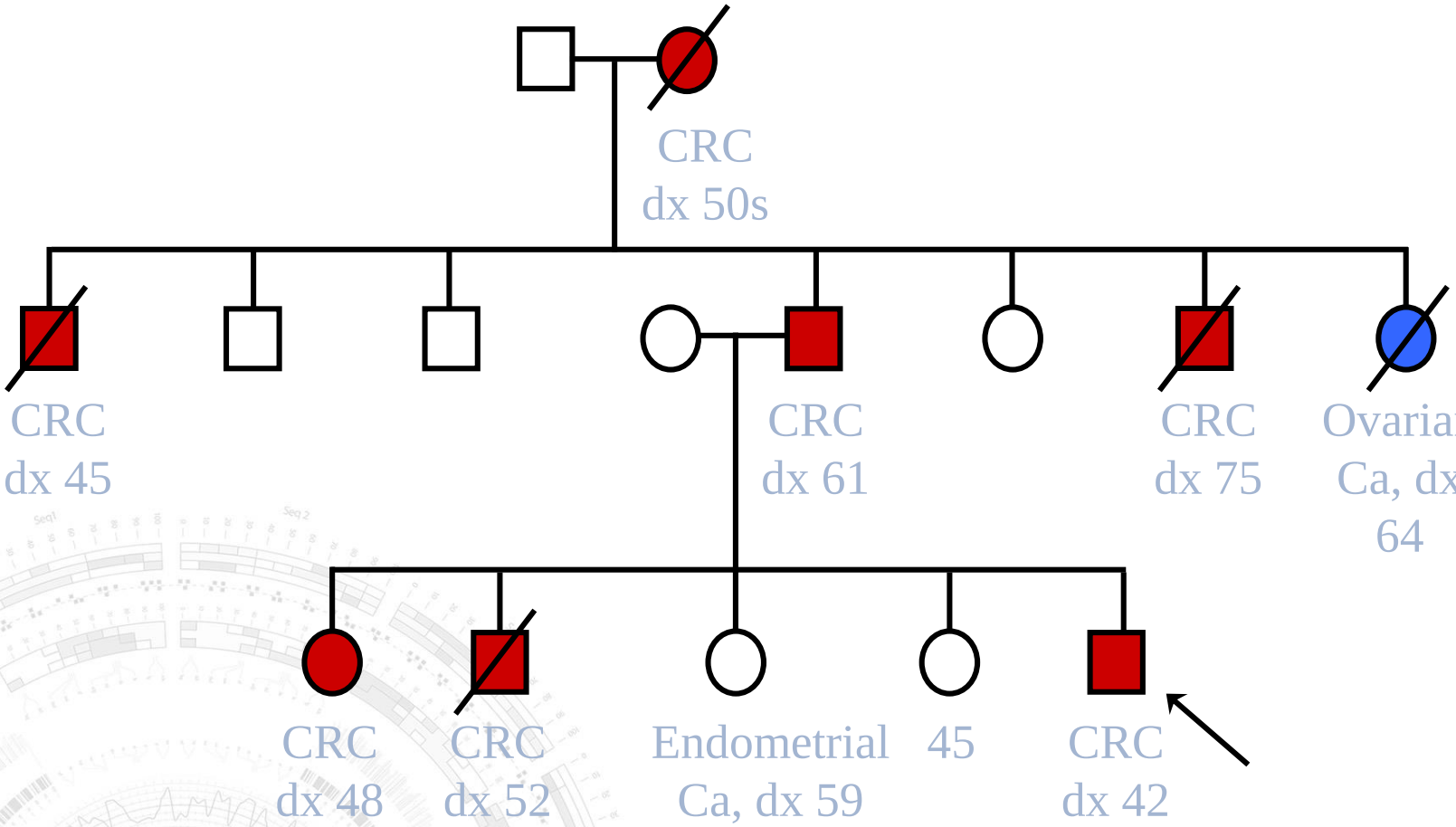
Lindor N et al. JAMA 2006;296:1507-17. & Vasen HFA et al. J Med Genet 2007;44:353-62

Lynch Syndrome Prophylactic Surgery Options

- Options include subtotal colectomy, hysterectomy, and oophorectomy
- Subtotal colectomy does not eliminate cancer risk
- Hysterectomy eliminates risk of endometrial and ovarian cancer
- Expert panels made no recommendation for or against surgery due to unproven efficacy

Schmeler et al. NEJM 2006;354:261-9.

Family history is an important component to diagnosing Lynch syndrome



The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Warning: Family Histories can be Deceiving

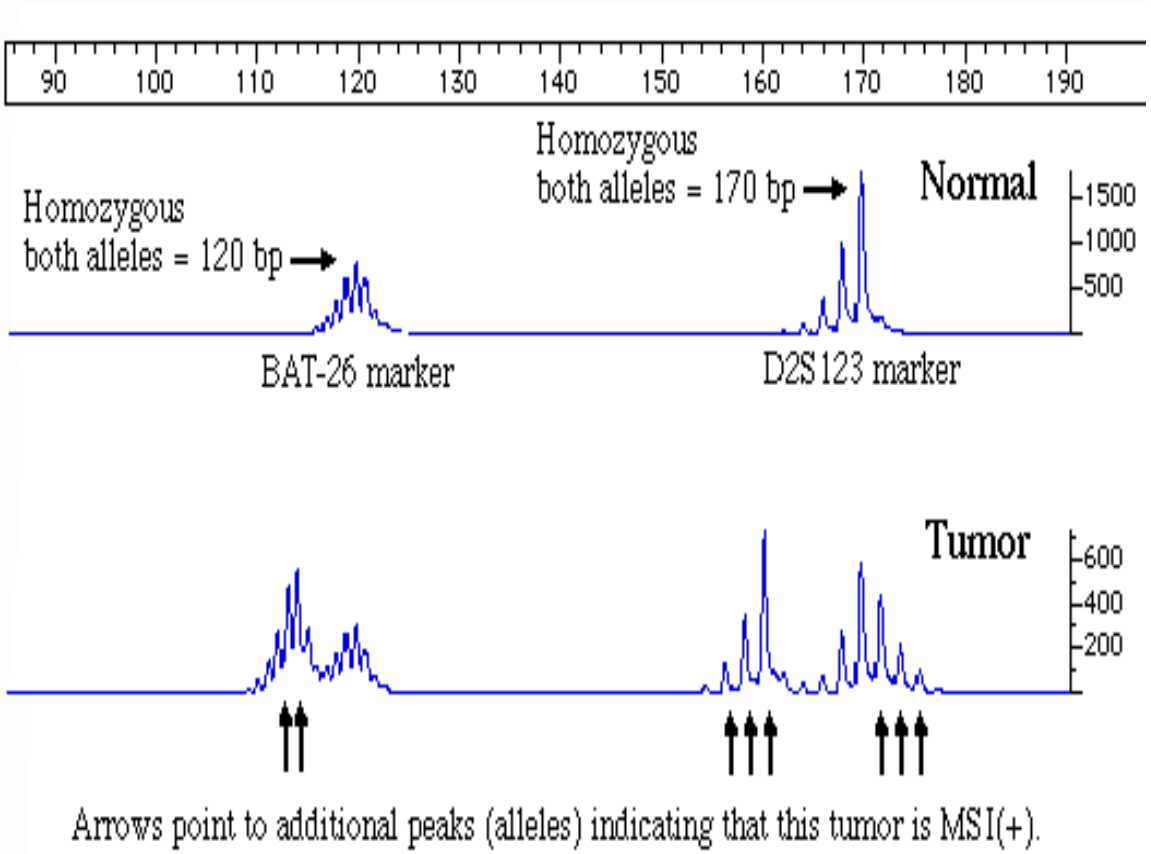
- Family size is getting smaller
- Wider use of colonoscopy likely to prevent many colon cancers
- MSH6 & PMS2 may have lower cancer risks

Genetic Features of Lynch Syndrome

- Genes belong to DNA mismatch repair (MMR) family
- Mutations in MMR genes lead to microsatellite instability
- MMR proteins are missing in the tumor tissue making immunohistochemical staining useful

Microsatellite Instability (MSI) testing

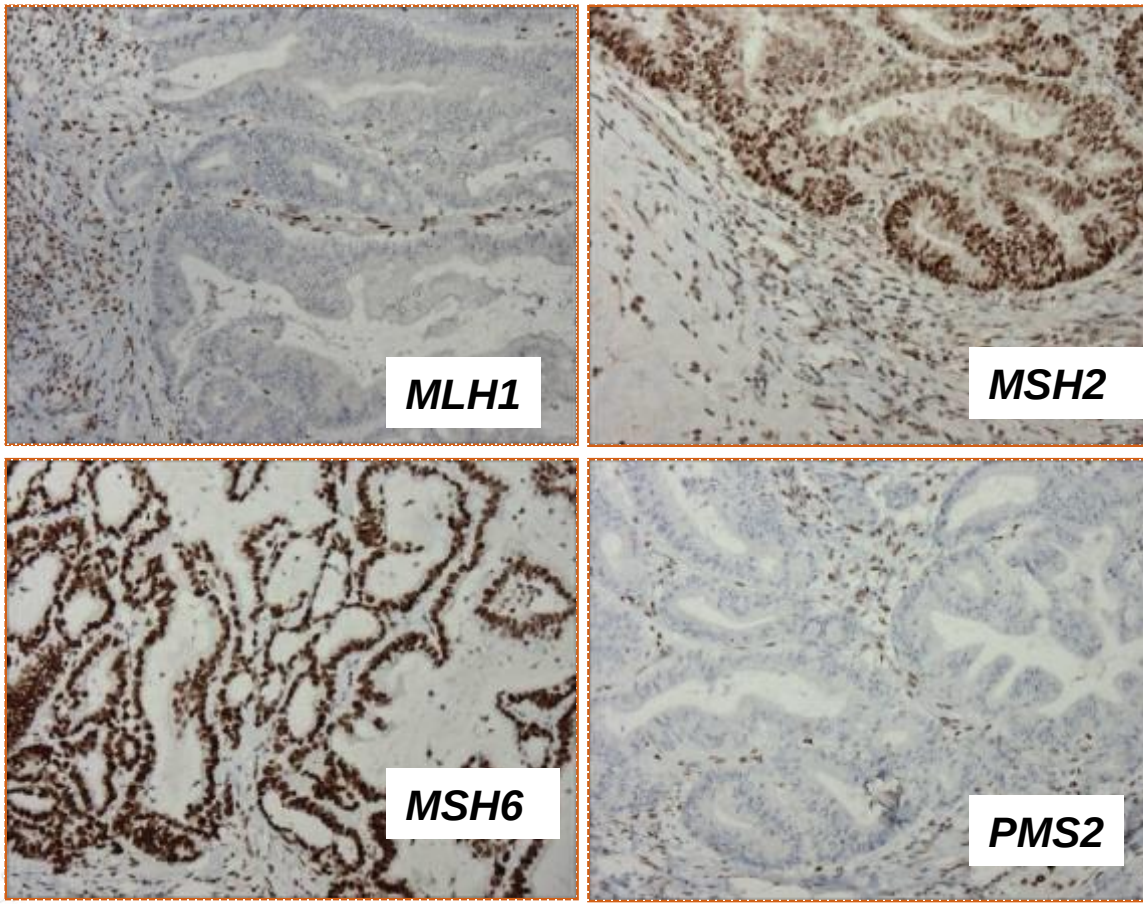
- Performed on DNA extracted from tumor and normal tissue – requires laboratory
- Test is positive in 15% of CRC cases
- Sensitivity is 77-89% of LS cases



Arrows point to additional peaks (alleles) indicating that this tumor is MSI(+).

Immunohistochemical (IHC) testing

- Performed on thin slide of tumor – can be done in pathology department
- All 4 proteins present 80% of the time
- 1-2 proteins absent 20% of the time
- Sensitivity is 83%



Potential Impact

- 132,700 new cases of CRC in the US in 2015
- 4,000 have Lynch syndrome (3%)
- 12,000 of their relatives have LS (~3 per proband)
- 54,870 new cases of EC in the US in 2015
- 1,650 have Lynch syndrome (3%)
- 3,300 of their relatives have LS (~2 per proband)
- Total of 21,000 individuals who could be diagnosed with LS this year with universal screening

Clinical Translation

- Studies have shown that universal tumor screening for Lynch syndrome is cost effective
- ICER of $31,391 per life year gained
- Universal tumor screening for Lynch syndrome is recommended by:
  - Evaluation of Genetic Applications in Practice & Prevention (CDC) since 2009
  - NCCN since 2013
  - US Multi-society Task Force on CRC since 2014
  - Society for Gynecologic Oncology & ACOG since 2014

Mvundura et al, Genet Med 2010;12:93-104; Grosse et al, Genetic in Med 2015;17;510-11; EGAPP, Genet Med 2009;11:35-41; Giardiello et al, Am J Gastroenterol 2014;109:1159-79; ACOG & SGO Practice Bulletin Number 147, 2014



Adoption of UTS for LS

Type of Institution	% Performing UTS
NCI-Comprehensive Cancer Centers	71%
COS-accredited Community Hospital Comprehensive Cancer Programs	36%
Community Hospital Cancer Programs	15%

Beamer et al, JCO 2012;30(10):1058-63.

Barriers to Implementing UTS for LS

- Lack of Knowledge/Interest in UTS for LS
- Lack of Genetic Counseling services
- Financial
  - High Medicare payer mix - DRG
- Internal Challenges
  - Can abnormal results be given to Genetics (HIPAA)?
  - Should all cases be screened or a subset?
  - Inability to do tests in house
  - Personalities

Efforts to Overcome these Barriers

- Lynch Syndrome Screening Network
  - Share Resources, Protocols & Data
  - Measure Success
- Public Health Approach
  - Use newborn screening type approach

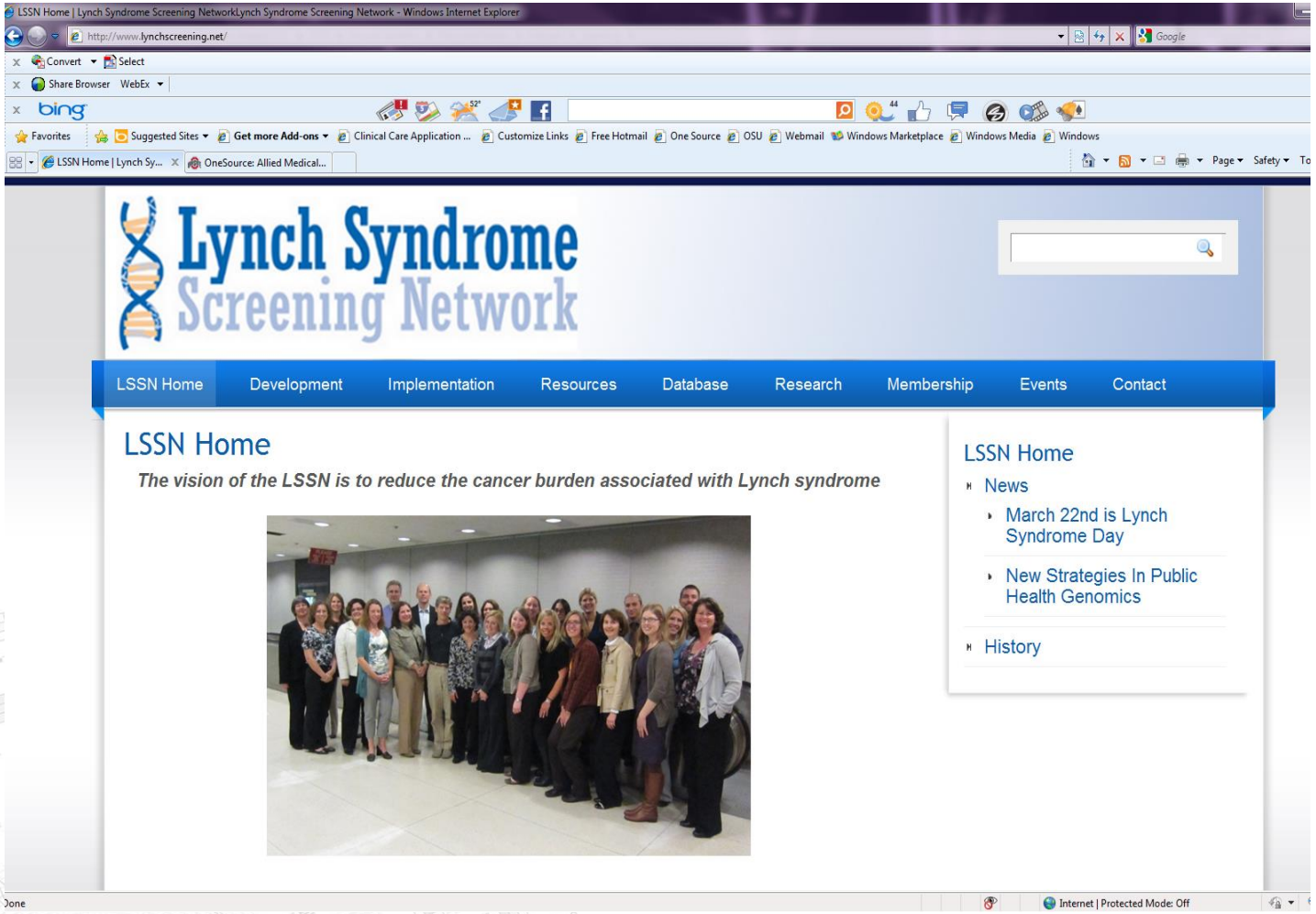
Hampel & de la Chapelle. Familial Cancer. 2013;12:313-17.

Lynch Syndrome Screening Network

- Created in September 2011
- **LSSN Mission:**

  To promote universal Lynch syndrome screening on all newly diagnosed colorectal and endometrial cancers; to facilitate the ability of institutions to implement appropriate screening by sharing resources, protocols and data through network collaboration; and to investigate universal screening for other Lynch syndrome related malignancies

LSSN Website: www.lynchscreening.net



The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Main goal: Develop a statewide cancer research infrastructure accounting for long term follow up

Goal: 3,000 CRC patients and 6,000+ first-degree relatives in 48 months
Start Date: 1/1/2013 at OSU, 3/1/13 at outside hospitals (majority)

Research Project 1

Universal Screening for Lynch Syndrome



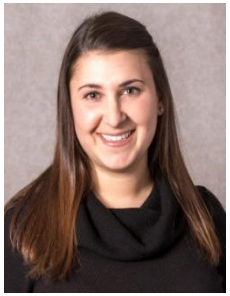
Albert de la Chapelle



Heather Hampel



Richard Goldberg



Rachel Pearlman

Research Project 2

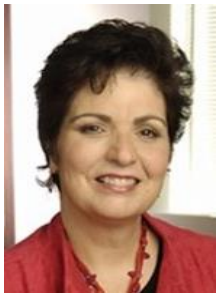
Molecular Epidemiology of Colorectal Cancer



Peter Shields

Research Project 3

Adherence to Colorectal Cancer Screening



Electra Paskett

Supported by Pelotonia

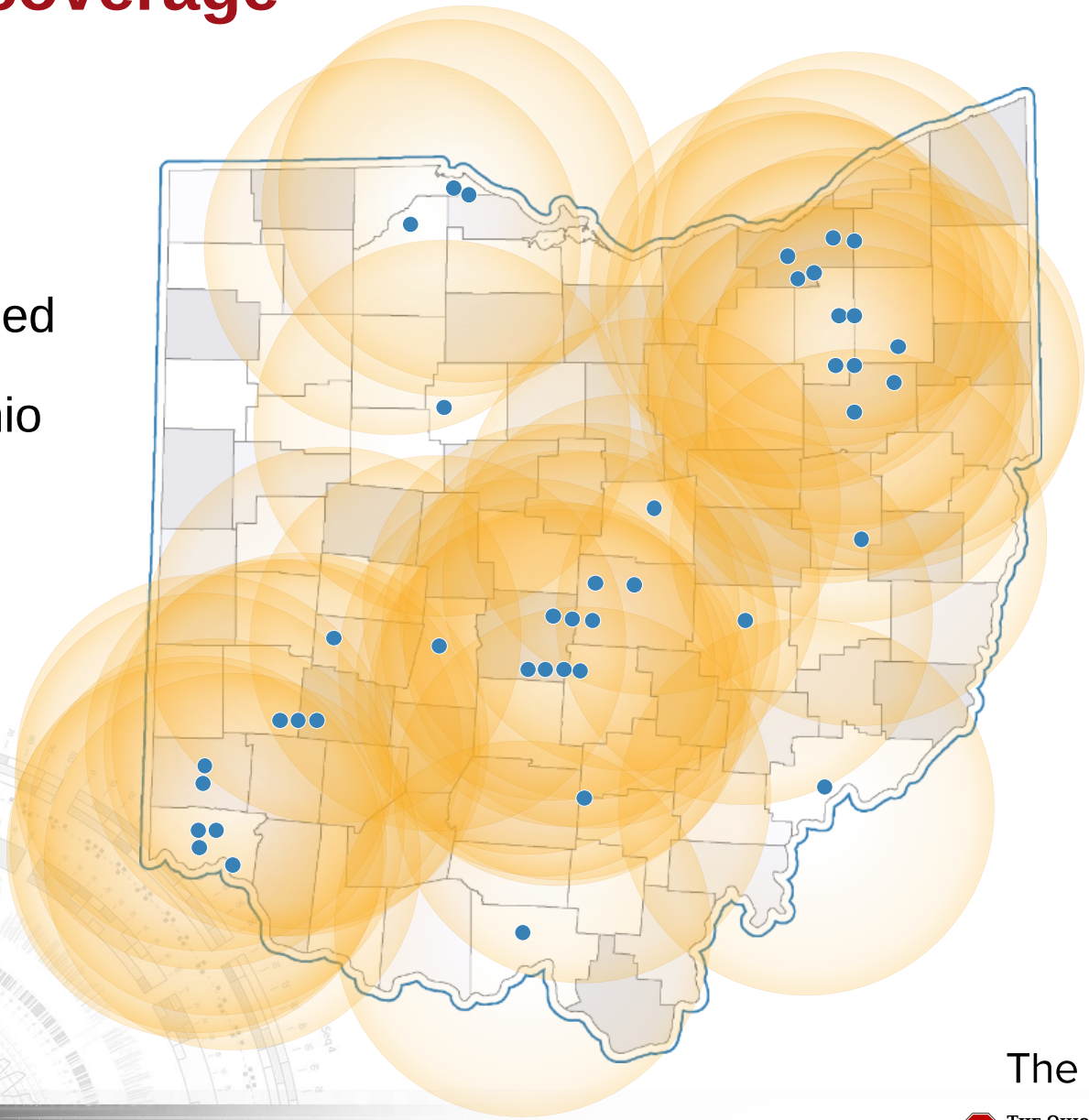
The James

The Ohio State University
Comprehensive Cancer Center

Statewide coverage

- Participating hospital N=51

  Patients enrolled from **84/88** counties in Ohio



The James

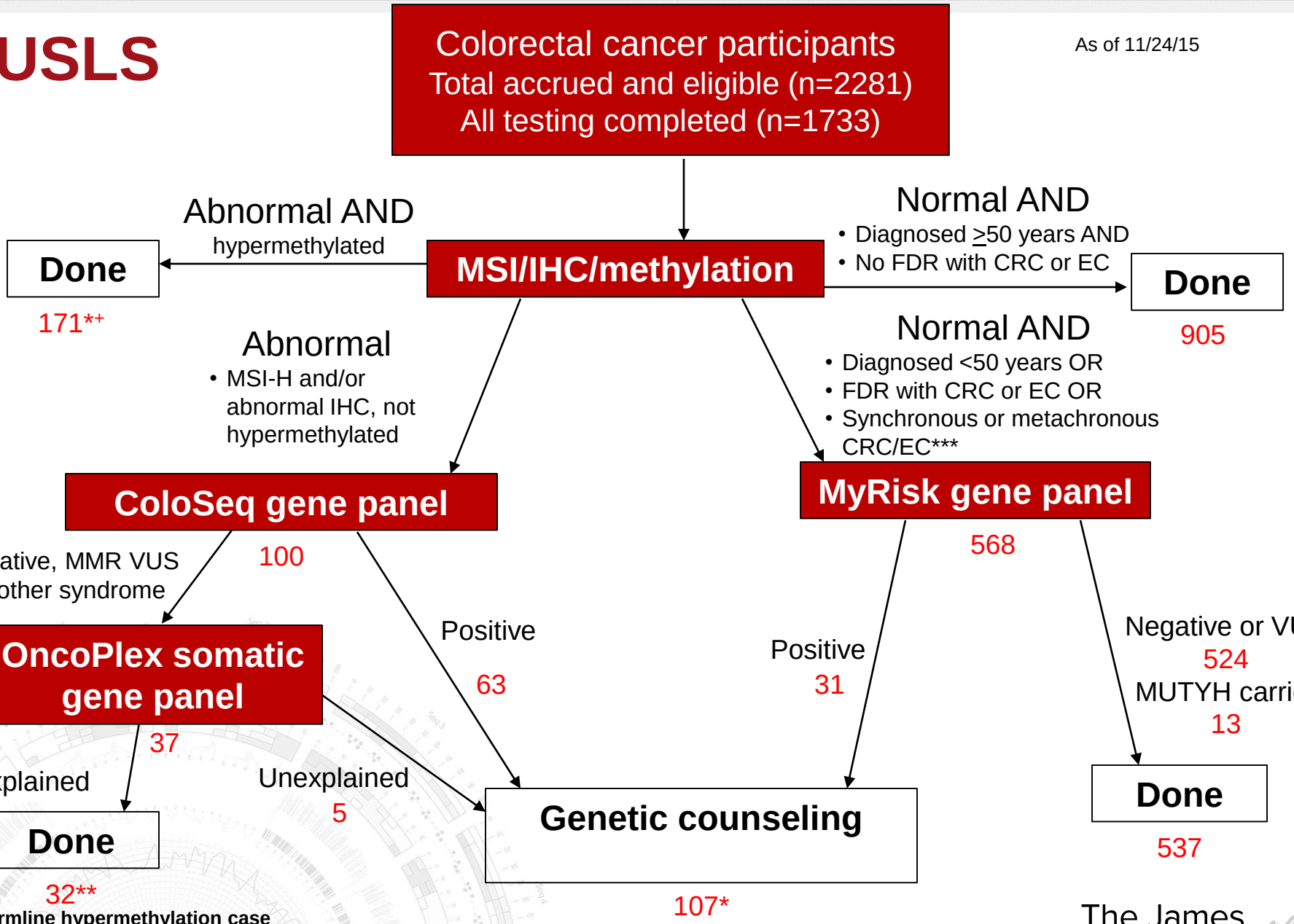
The Ohio State University
Comprehensive Cancer Center

Participating Hospitals

OCCPI Participating Hospitals	
Cleveland Clinic Foundation (Cleveland)	**Fairfield Medical Center** (Lancaster)
OSUMC/James (Columbus)	Adena Health System (Chillicothe)
Riverside Methodist Hospital (Columbus)	Springfield Regional Medical Center (Springfield)
The Christ Hospital (Cincinnati)	Blanchard Valley Regional Health Center (Findlay)
Mount Carmel East (Columbus)	Upper Valley Medical Center (Troy)
Summa Akron City/St. Thomas Hospital (Akron)	Atrium Medical Center (Middletown)
Aultman Hospital (Canton)	ProMedica St. Luke's Hospital (Maumee)
Kettering Medical Center (Dayton)	Robinson Memorial Hospital (Ravenna)
Miami Valley Hospital (Dayton)	Mount Carmel St. Ann's (Westerville)
Bethesda North Hospital- TriHealth (Cincinnati)	Southern Ohio Medical Center (Portsmouth)
ProMedica Toledo Hospital (Toledo)	Grant Medical Center (Columbus)
Hillcrest Hospital (Mayfield Heights)	Marietta Memorial Hospital (Marietta)
Mount Carmel West (Columbus)	Summa Barberton Hospital (Barberton)
St. Rita's Medical Center (Lima)	Doctors Hospital West (Columbus)
Good Samaritan Hospital- TriHealth (Cincinnati)	Licking Memorial Hospital (Newark)
MetroHealth System (Cleveland)	Knox Community Hospital (Mount Vernon)
Genesis Healthcare System (Zanesville)	Grady Memorial Hospital (Delaware)
ProMedica Flower Hospital (Sylvania)	Summa Western Reserve (Cuyahoga Falls)
Fairview Hospital (Cleveland)	Wayne Hospital (Greenville)
Good Samaritan Hospital (Dayton)	Mercy Medical Center (Canton)
Akron General Medical Center (Akron)	Wright-Patterson Medical Center (WPAFB)

USLS

As of 11/24/15

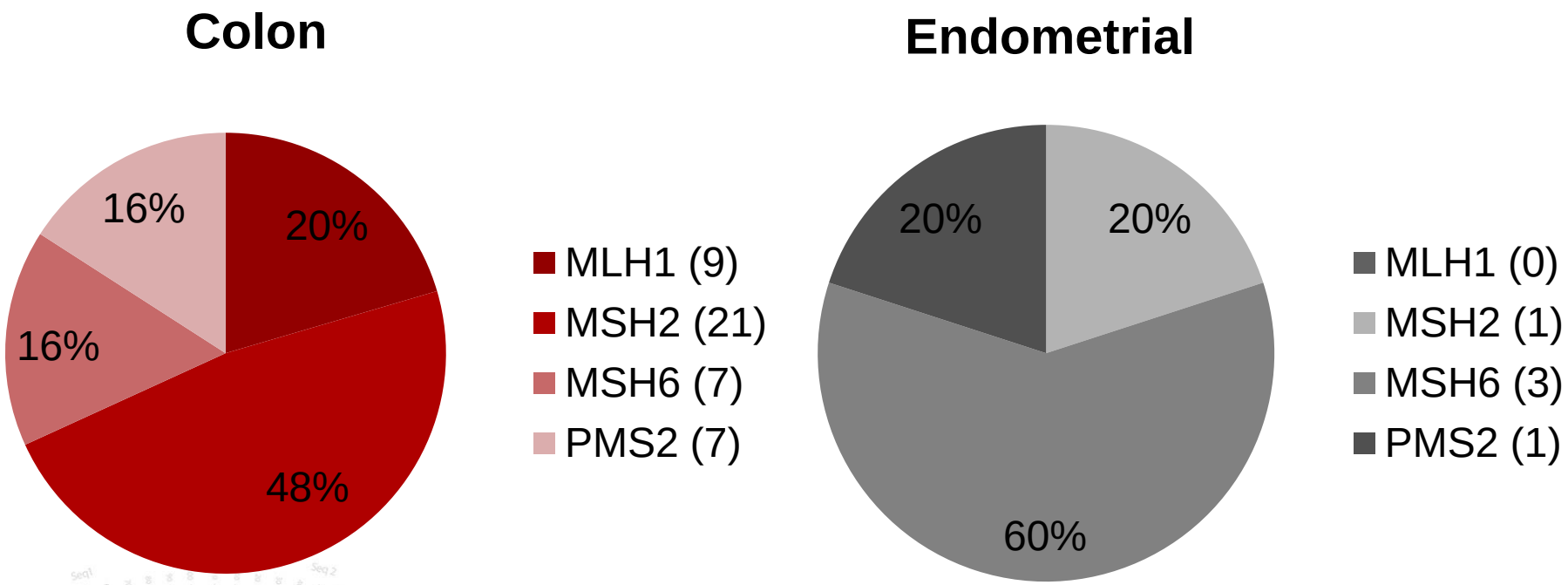


***1 germline hypermethylation case**
+10 "likely" hypermethylated (BRAF+, insufficient for methylation)
****4 MMR VUS reclassified to likely pathogenic, 2 biallelic MUTYH and double somatic, 26 double somatic**
*****11 cases double counted because they are methylated but synch/met primary → MyRisk**

The James

The Ohio State University
Comprehensive Cancer Center

Participants with Lynch Syndrome



- **As of 4/17/2015, 49 patients (44 colon, 5 endometrial) have been diagnosed with Lynch syndrome.**
- **31% had a known mutation or known mutation in the family but hadn't had testing themselves (15/49).**

Family Studies

Altogether we have diagnosed 102 CRC patients and 53 relatives (155 people) with an actionable hereditary cancer susceptibility syndrome in 35 months.

68/71 CRC Lynch probands have had genetic counseling.

40/71 have family members enrolled.

Degree of Kinship	Tested	Positive	Pending
First	77	32	3
Second	27	10	2
> Second	37	11	0
Total	141	53	5

Prescription

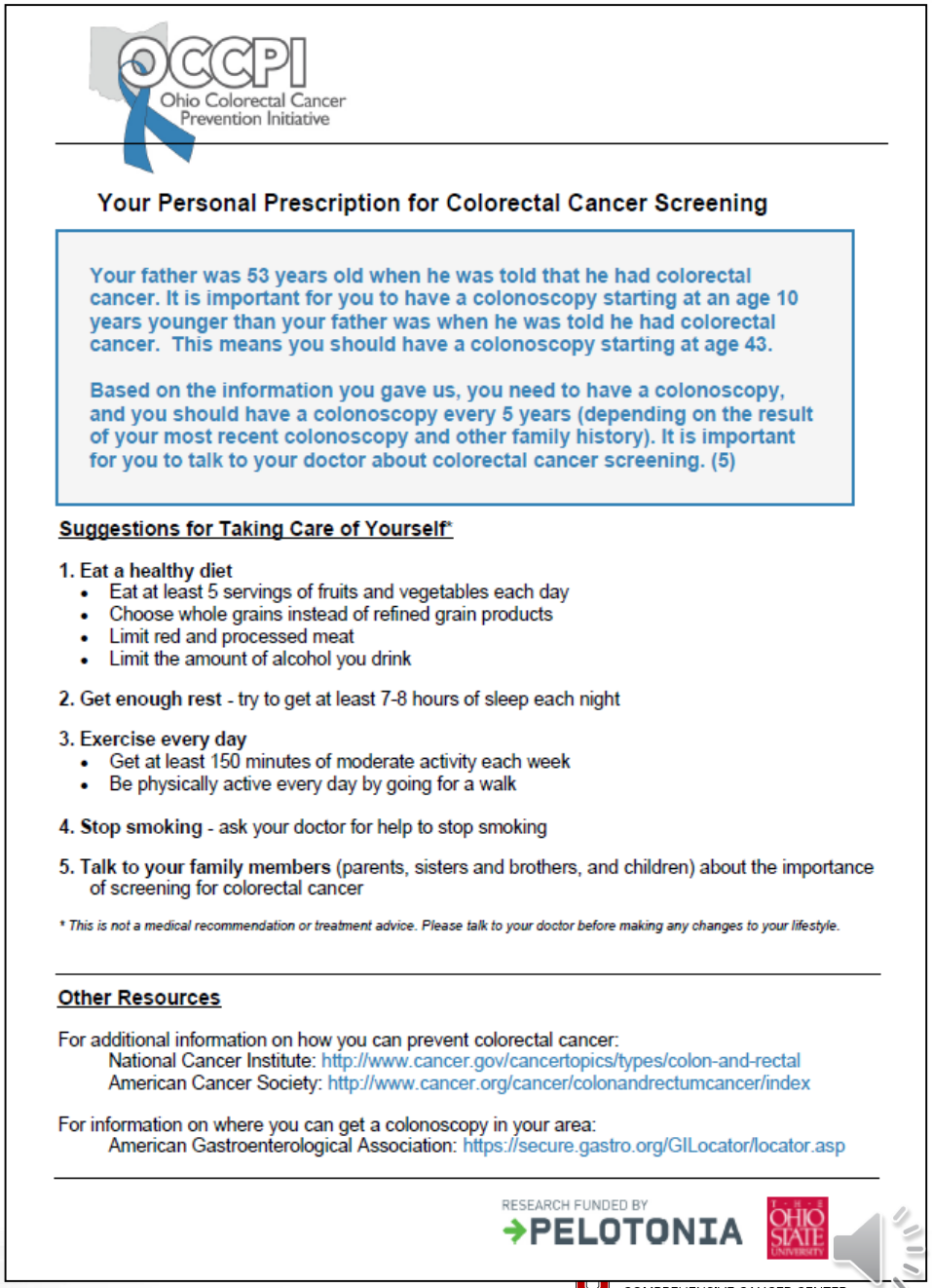
Tailored CRC screening message:

For CRC survivors:

- Pre-operative colonoscopy completion
- Type of operation

First Degree Relatives:

- Age of participant
- Age their relative was diagnosed with CRC
- Previous CRC screening



OCCPI Ohio Colorectal Cancer Prevention Initiative

Your Personal Prescription for Colorectal Cancer Screening

Your father was 53 years old when he was told that he had colorectal cancer. It is important for you to have a colonoscopy starting at an age 10 years younger than your father was when he was told he had colorectal cancer. This means you should have a colonoscopy starting at age 43.

Based on the information you gave us, you need to have a colonoscopy, and you should have a colonoscopy every 5 years (depending on the result of your most recent colonoscopy and other family history). It is important for you to talk to your doctor about colorectal cancer screening. (5)

Suggestions for Taking Care of Yourself*

1. **Eat a healthy diet**
   - Eat at least 5 servings of fruits and vegetables each day
   - Choose whole grains instead of refined grain products
   - Limit red and processed meat
   - Limit the amount of alcohol you drink
2. **Get enough rest** - try to get at least 7-8 hours of sleep each night
3. **Exercise every day**
   - Get at least 150 minutes of moderate activity each week
   - Be physically active every day by going for a walk
4. **Stop smoking** - ask your doctor for help to stop smoking
5. **Talk to your family members** (parents, sisters and brothers, and children) about the importance of screening for colorectal cancer

** This is not a medical recommendation or treatment advice. Please talk to your doctor before making any changes to your lifestyle.*

Other Resources

For additional information on how you can prevent colorectal cancer:
National Cancer Institute: http://www.cancer.gov/cancertopics/types/colon-and-rectal
American Cancer Society: http://www.cancer.org/cancer/colonandrectumcancer/index

For information on where you can get a colonoscopy in your area:
American Gastroenterological Association: https://secure.gastro.org/GILocator/locator.asp

RESEARCH FUNDED BY PELOTONIA

THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER

Navigation Activities

- Assess screening barriers
- Provide counseling to address screening barriers
- Provide assistance with any scheduling issues

If *CRC screening is recommended*:

- Offer encouragement to talk to doctor about scheduling a test
- Stress the importance of getting screened
- Address any barriers to getting screened
- Offer support and assistance

If *CRC screening or follow-up care is not recommended*:

- Suggest discussing results with their doctor
- Remind them of the importance of being screened or completing follow-up care according to NCCN recommendations.

- May make periodic follow-up calls to check on progress regarding scheduling and completing the screening, and to provide further assistance and support.

The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Recruitment To Date

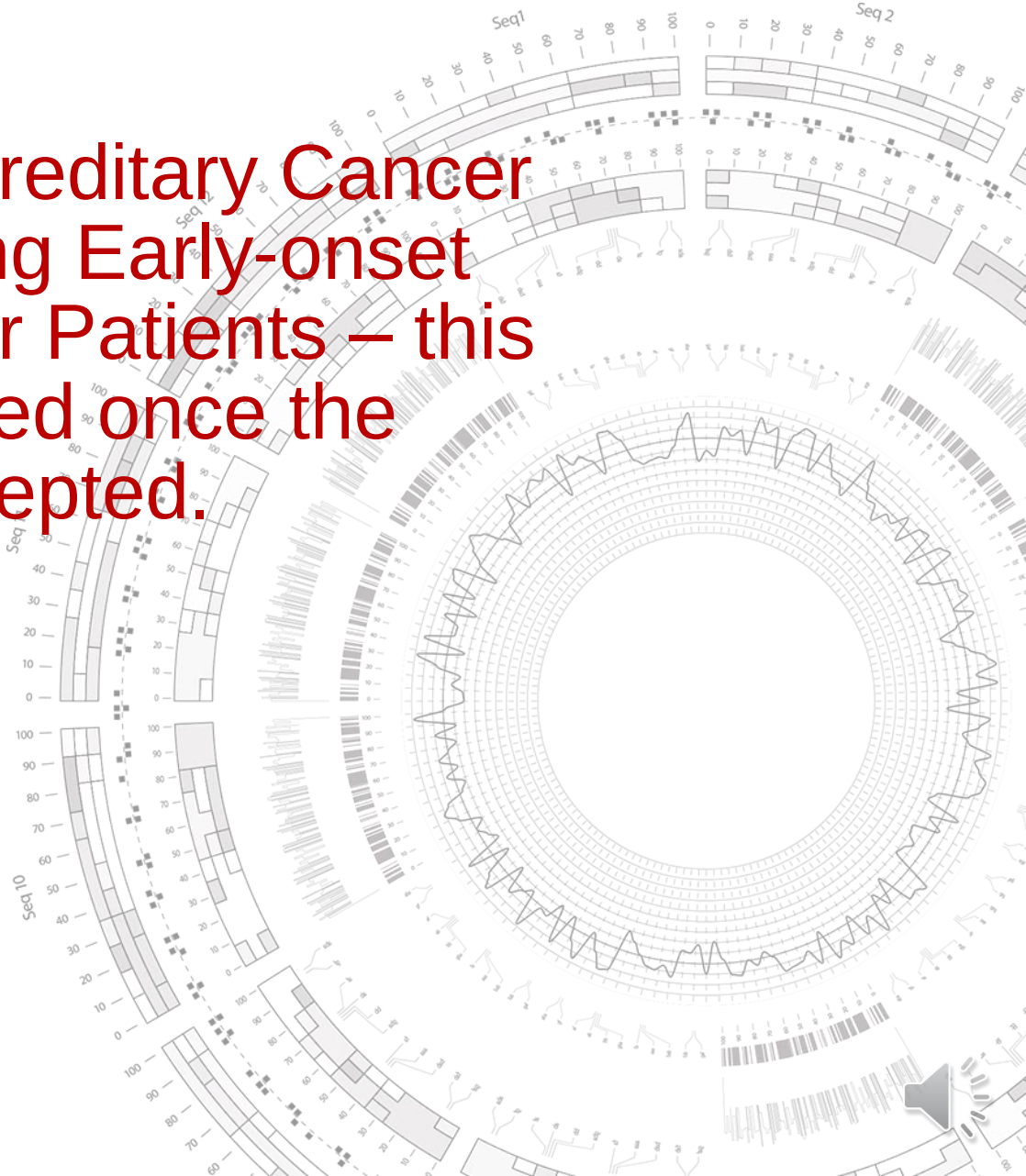
- Lynch Negative Probands = 653
- Lynch Negative FDR's = 732
- Lynch Positive Probands = 32
- Lynch Positive FDR's = 21
- Total Recruited = 1438

The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

MECC

- Participation
  - 2202 (96.5%) CRC participants consented to MECC
    - 79 declined MECC
  - 466 relatives consented to MECC
    - FDRs of LS- probands
    - At-risk relatives of LS+ probands (FDR, SDR, TDR, etc)
- Accrual
  - CRC probands: 858
  - EC probands: 119
  - FDRs of Lynch positive probands: 43
  - FDRs of non-LS CRC probands: 108
  - Total completed = 1128

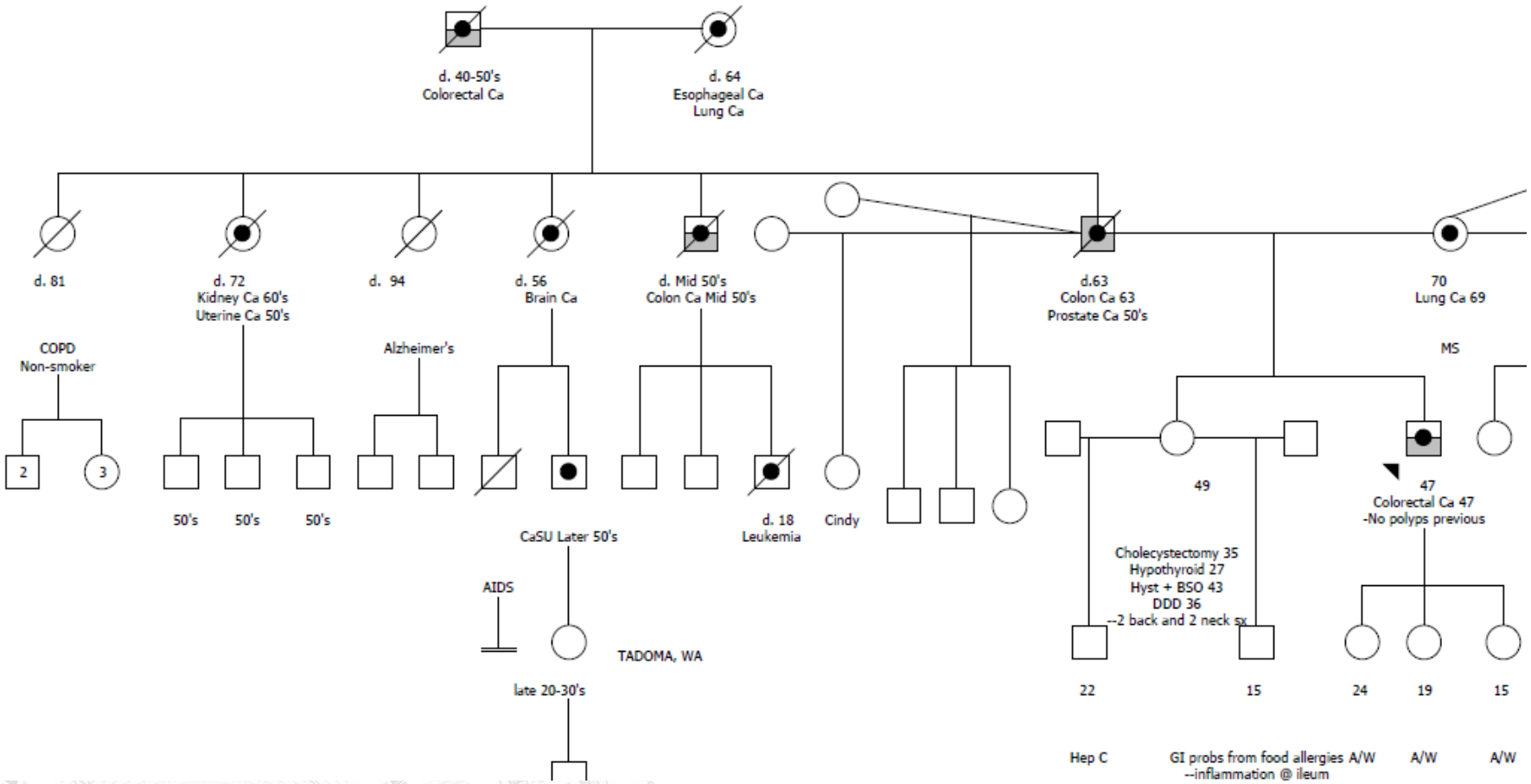
Prevalence of Hereditary Cancer Syndromes among Early-onset Colorectal Cancer Patients – this slides will be added once the publication is accepted.



The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

First patient diagnosed with Lynch syndrome in OCCPI



The James

THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

A legacy of cancer





Father

The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

Cascade testing



- Family Reunion June 2014
- On Mississippi River in western Kentucky
- Tested 20 at-risk relatives from his dad's side of the family
- Found one additional branch of family with Lynch syndrome
- They can now participate in live-saving cancer surveillance

The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER


The James
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER
A CANCER-FREE WORLD
BEGINS HERE