Integrating Genetic and Genomic Medicine Processes For Systematic Identification of Neoplasias

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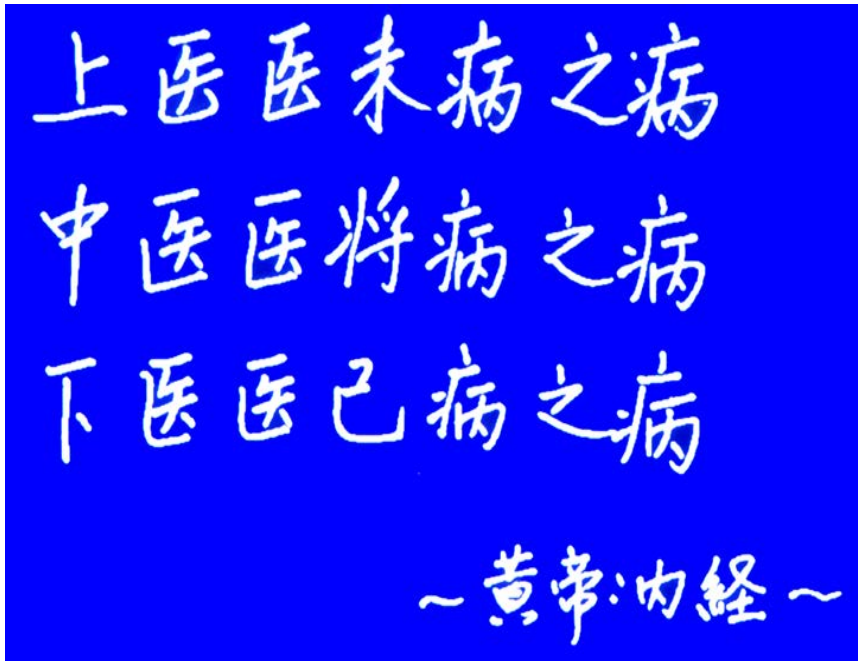
NHGRI Genomic Medicine Colloquium, Dec 5, 2011, 11 AM Session

Historical Imperative for Prevention



Superior doctors prevent the disease.

Mediocre doctors treat the disease before evident.

Inferior doctors treat the full blown disease.

Nai-Ching (2600 B.C. 1st Chinese Medical Text)

June, 2011 Genomic Medicine Colloquium (Chicago)

- MSI Analysis and Mismatch Repair Protein IHC for Lynch Syndrome Screening for All Resected Colorectal Cancers on Main Campus (80% Uptake to Genetics Clinics)
- Implementation of MSI Analysis and Mismatch Repair Protein IHC for Lynch Syndrome Screening for All Endometrial Cancers on Main Campus (64% Uptake and Challenges)
- Integration of Genetic Counselors in >25 Non-Genetics Specialty Clinics on Main Campus and Regional Practice
- Prototype of Patient-Entered Cancer Family History Web-Based Tool

Today: Routine Screening for Heritable Pheochromocytoma and Paragangliomas

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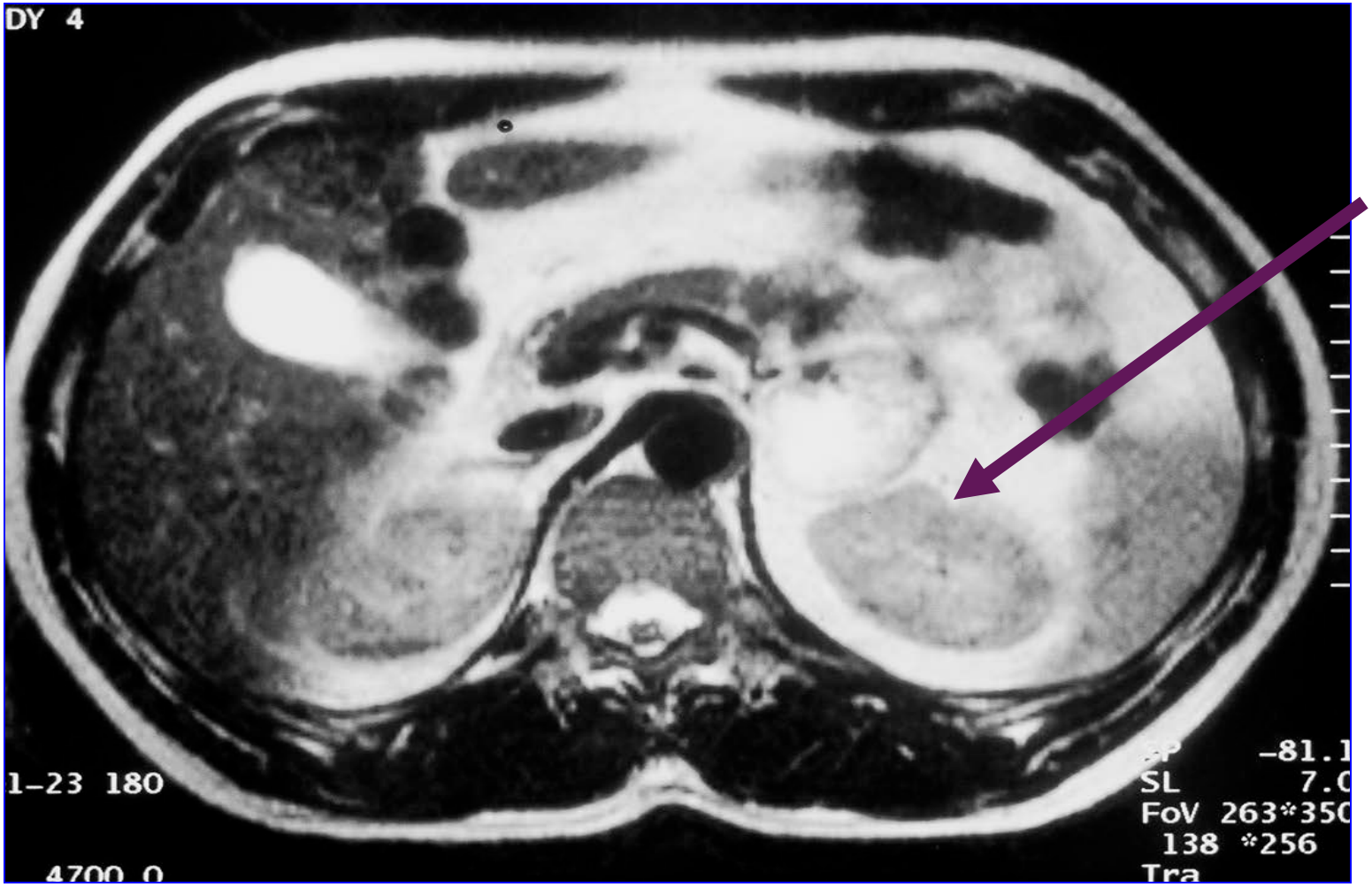
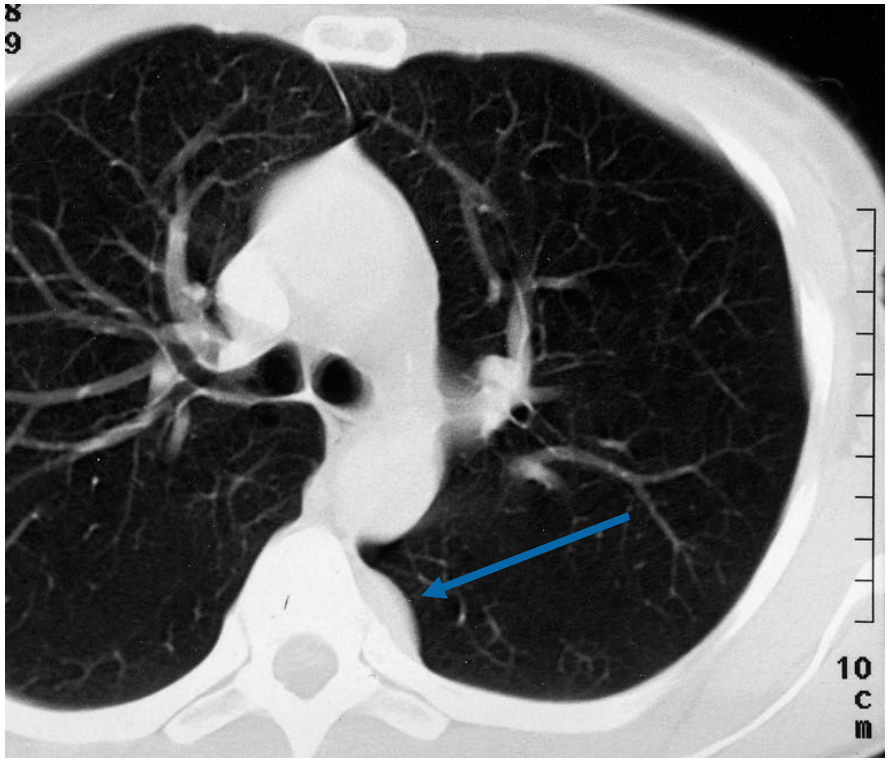
Pheochromocytoma: Prototype Neuroendocrine Tumor

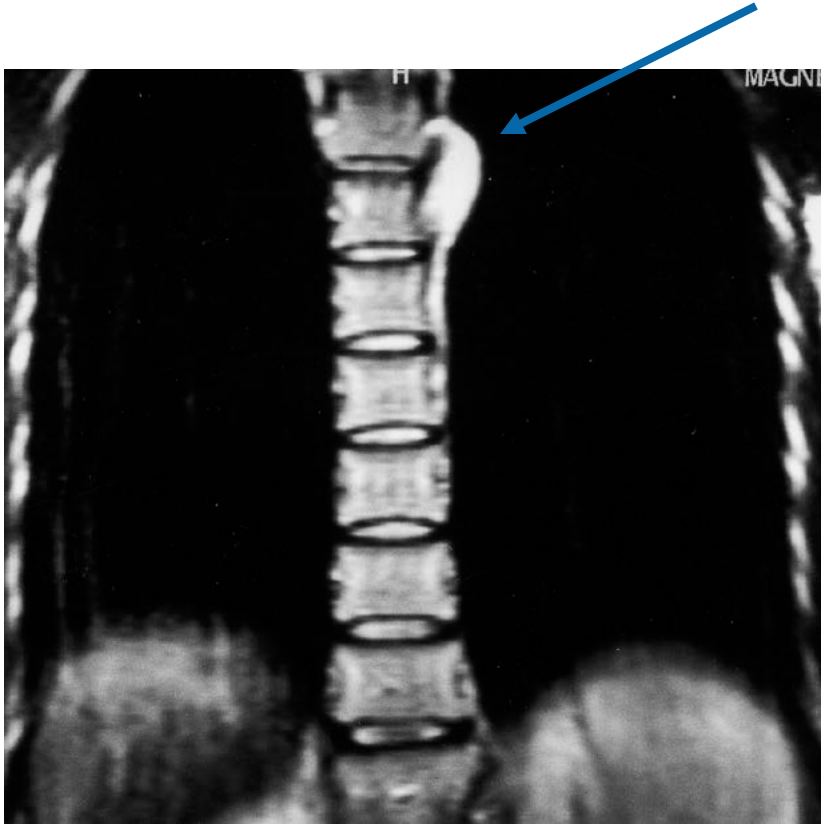
- Pheochromocytoma (Pheo)
- Tumor of Adrenal Medulla
  - Chromaffin Cells (Neural Crest)
  - Can Secrete Catecholamines
    - Hypertension
    - Headache, Palpitations, Pallor, Etc
    - Stroke, Sudden Death

Pheochromocytoma: Neoplasia of Adrenal Medulla

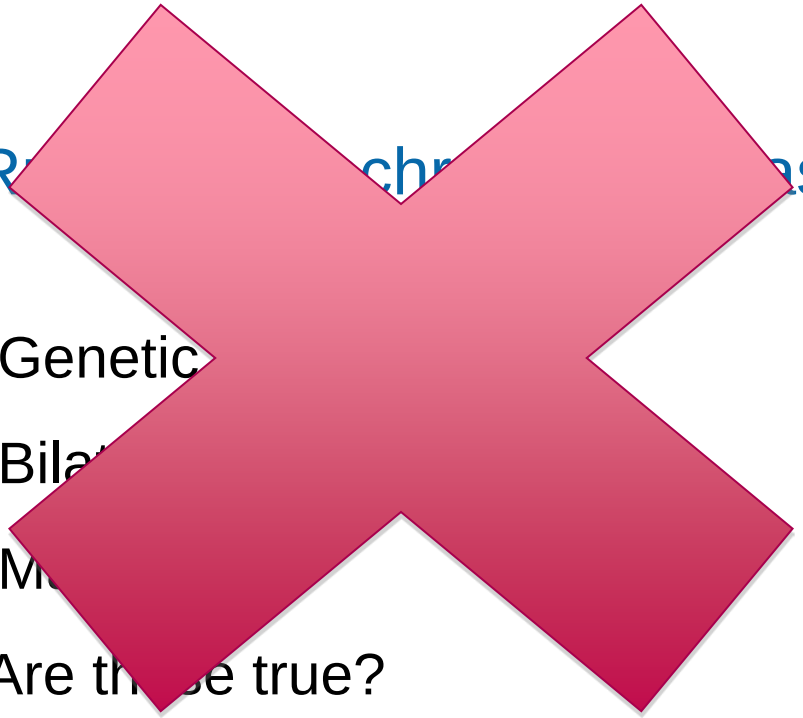


Paraganglioma (Extra-Adrenal Pheo)





10% R… chr…as

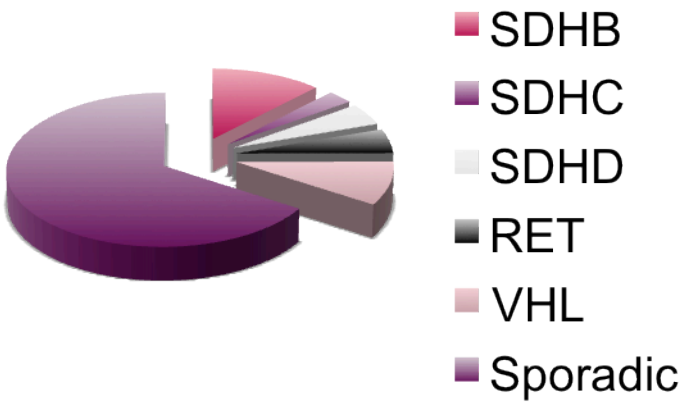


- 10% Genetic
- 10% Bila…
- 10% M…
- But: Are th…e true?
- Does it matter?
  - –Would it affect patient care?

Approximately 20-30% of All Pheo and PGL Presentations Have Genetic Etiology (Germline Mutations)

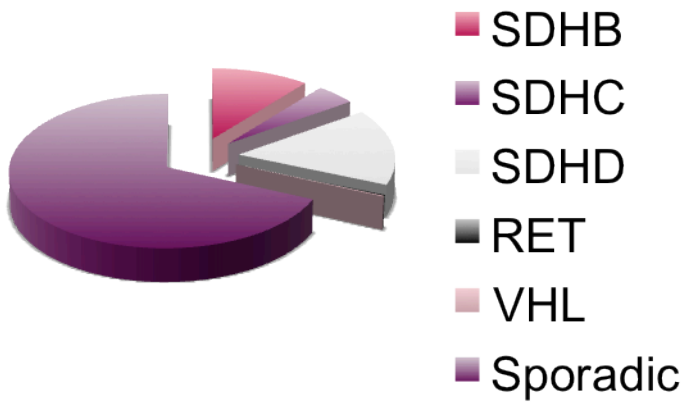
989 PC

20% Carry Germline Mutations



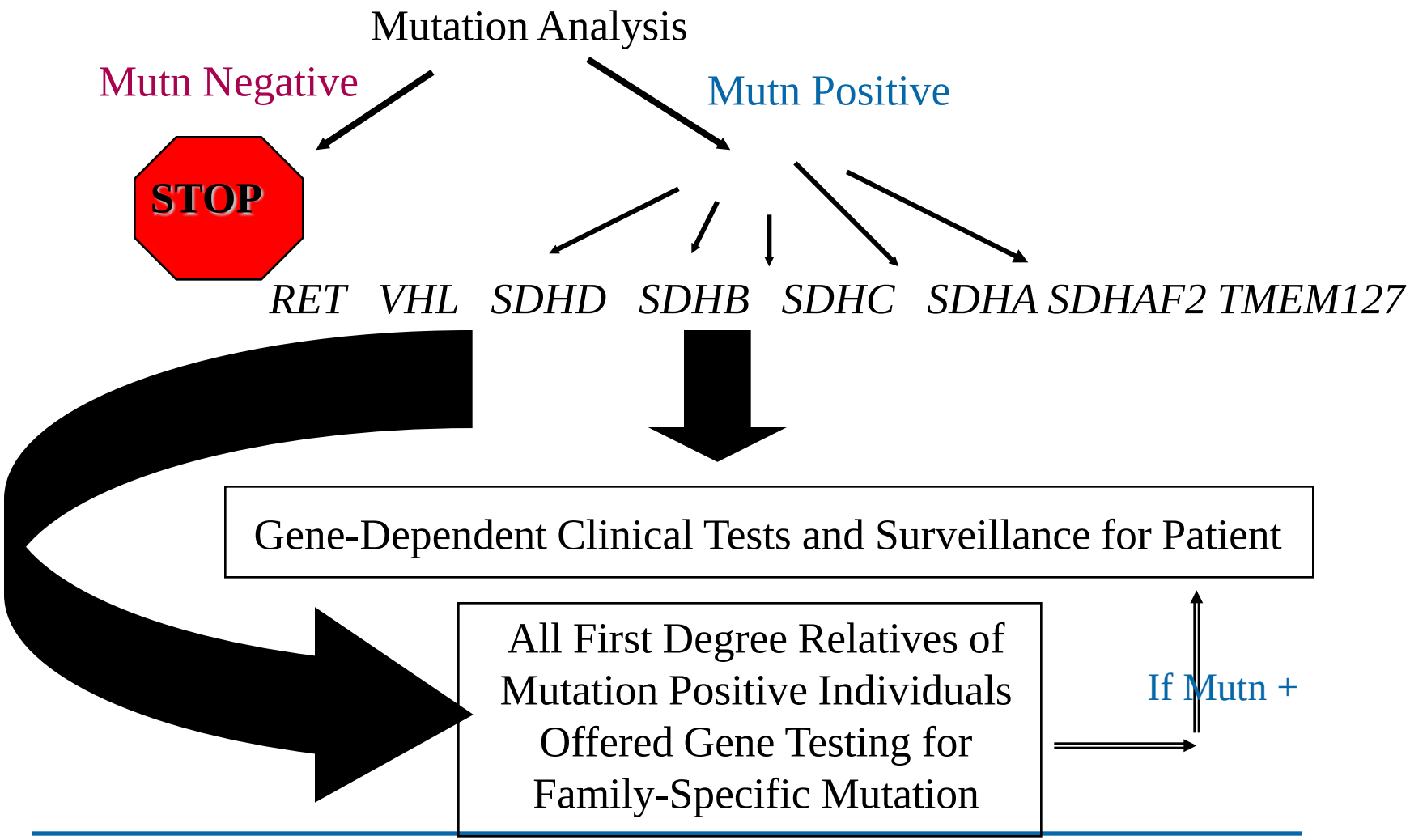
600 PGL

30% Carry Germline Mutations



Neumann et al. *NEJM 2002, JAMA 2004, Cancer Res 2009,*
Schiavi et al. *JAMA 2005,* Erlic et al. *Clin Cancer Res 2009*

Gene-Specific Neoplasia Risks Guide Management

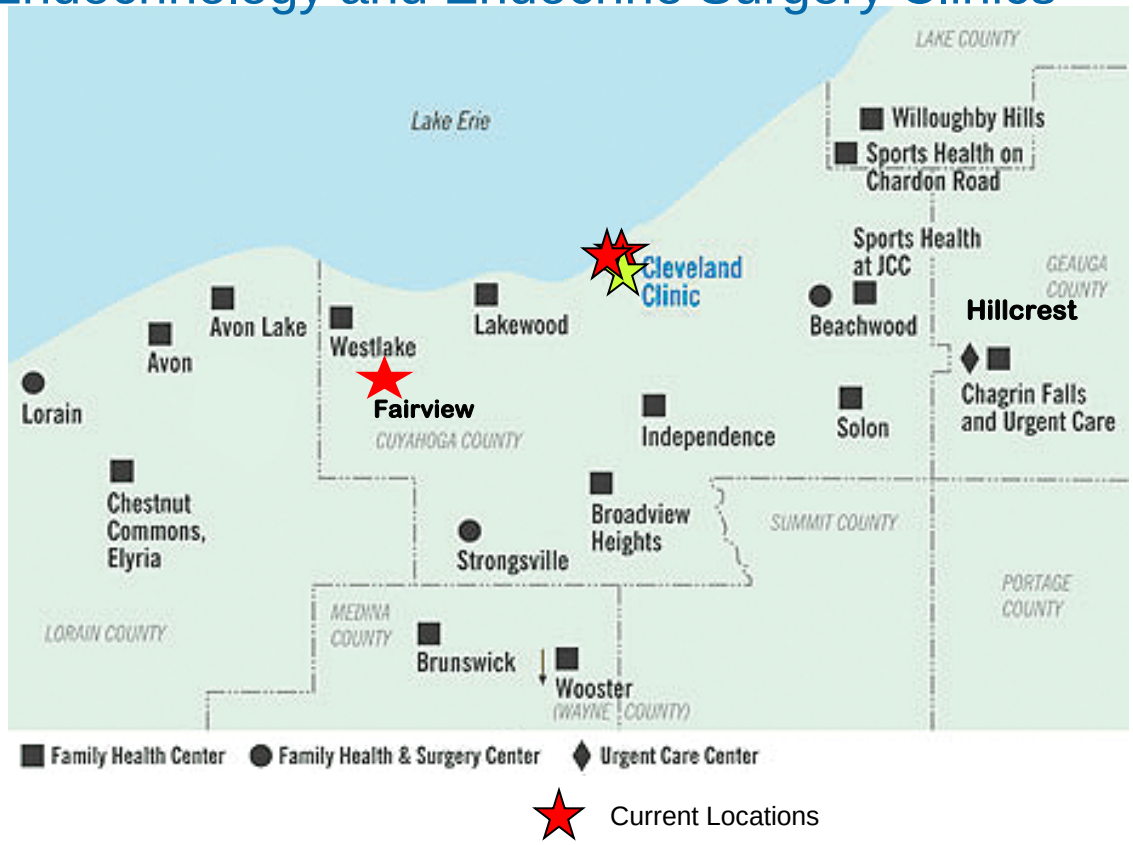


Genomic Medicine Institute
Center for Personalized Genetic Healthcare

Have Embedded Genetic Counselor in Main Campus Endocrinology and Endocrine Surgery Clinics

Lou Ruvo

CC Abu Dhabi



CC Canada

CC Florida

SDHx Immunohistochemistry Screen?

- SDHB Null by IHC in PC and PGL with Germline *SDHB, SDHC* or *SDHD* Mutation
  - SDHB Expressed in Those with MEN 2, VHL and NF 1
- 6/316 PC/PGL SDHA Null by IHC – Germline *SDHA* Mutations
- Routinely Implemented at PennNET
- BUT: Cleveland Clinic Clinical Pathologists Inconsistent Results
  - My Lab: Blind Reading of SDHB Western Blot from Tumors from those With and Without Germline *SDHx* Mutations
    - Completely Random “Calls”

Van Nederveen et al. *Lancet Oncol* 2009, Korperschoek et al. *JCEM 2011*