Greenwood Genetic Center

Founded in 1974 by the SC Department of Disabilities & Special Needs and the Self Family Foundation as a not-for-profit genetic institute.

Our Mission:

- ***Provide clinical genetic services***
- ***Offer a range of diagnostic testing services***
- ***Develop educational programs and materials***
- ***Conduct research in the field of medical genetics***

Greenwood Genetic Center

Where Compassion Inspires Progress

Agenda: An Overview of Genetic Evaluation and Testing

Our referral process and patient requirements – 5 min

Brian Albon, Clinical Operations Manager

What to Expect from a Genetic Evaluation: Part I – 10 min

Amy Dobson, MS, Genetic Counselor

What to Expect from a Genetic Evaluation: Part II – 20 min

Mike Lyons, MD, Director of Clinical Services

Genetic Testing Basics (Chromosomes/Array/Panels/Exomes) – 25 min

Mike Friez, PhD, Director of Diagnostic Labs

Questions and Discussion – As long as you want

Greenwood Genetic Center

Points of Contact

Locations

Greenwood
106 Gregor Mendel Circle Greenwood, SC 29646
Hours: 8am-5pm Monday - Friday
Phone: 864.941.8100
Toll Free: 888.GGC.GENE / 888.442.4363
Fax: 864-941-8114
Map

Greenville
14 Edgewood Dr. Greenville, SC 29605
Hours: 8am-5pm Monday - Friday
Phone: 864.250.7944
Toll Free: 866.478.4363
Fax: 864-250-9582
Map

Columbia
1911 Thurmond Mall Columbia, SC 29201
Hours: 8am-5pm Monday - Friday
Phone: 803.799.5390
Toll Free: 800.679.5390
Fax: 803-799-5391
Map

Charleston
3520 W. Montague Ave. Suite 104
North Charleston, SC 29418
Hours: 8am-5pm Monday - Friday
Phone: 843.746.1001
Toll Free: 866.588.4363
Fax: 843-735-5097
Map

Florence
Hours: By appointment only
Mailing address:
PO Box 4033
Florence, SC 29502
Phone: 843.746.1001

Our Offices' points of contact are listed to the right.

Additionally, questions specific to the referral process can be directed to:

Brian Albon: balbon@ggc.org

Abbey Quarles: aquarles@ggc.org

Debbie Bealer: dbealer@ggc.org

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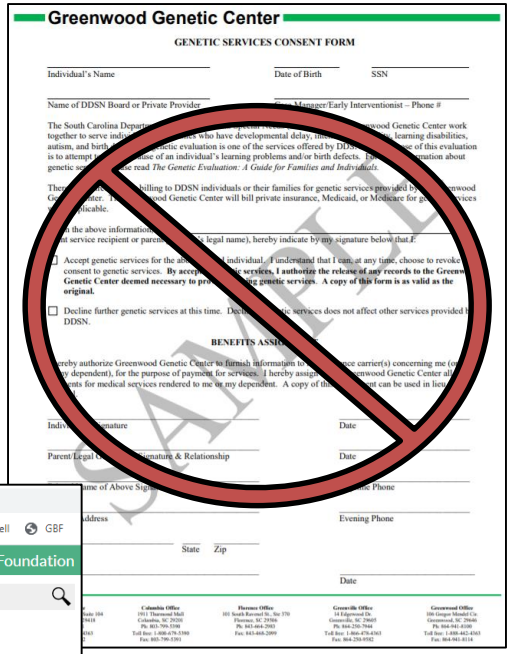
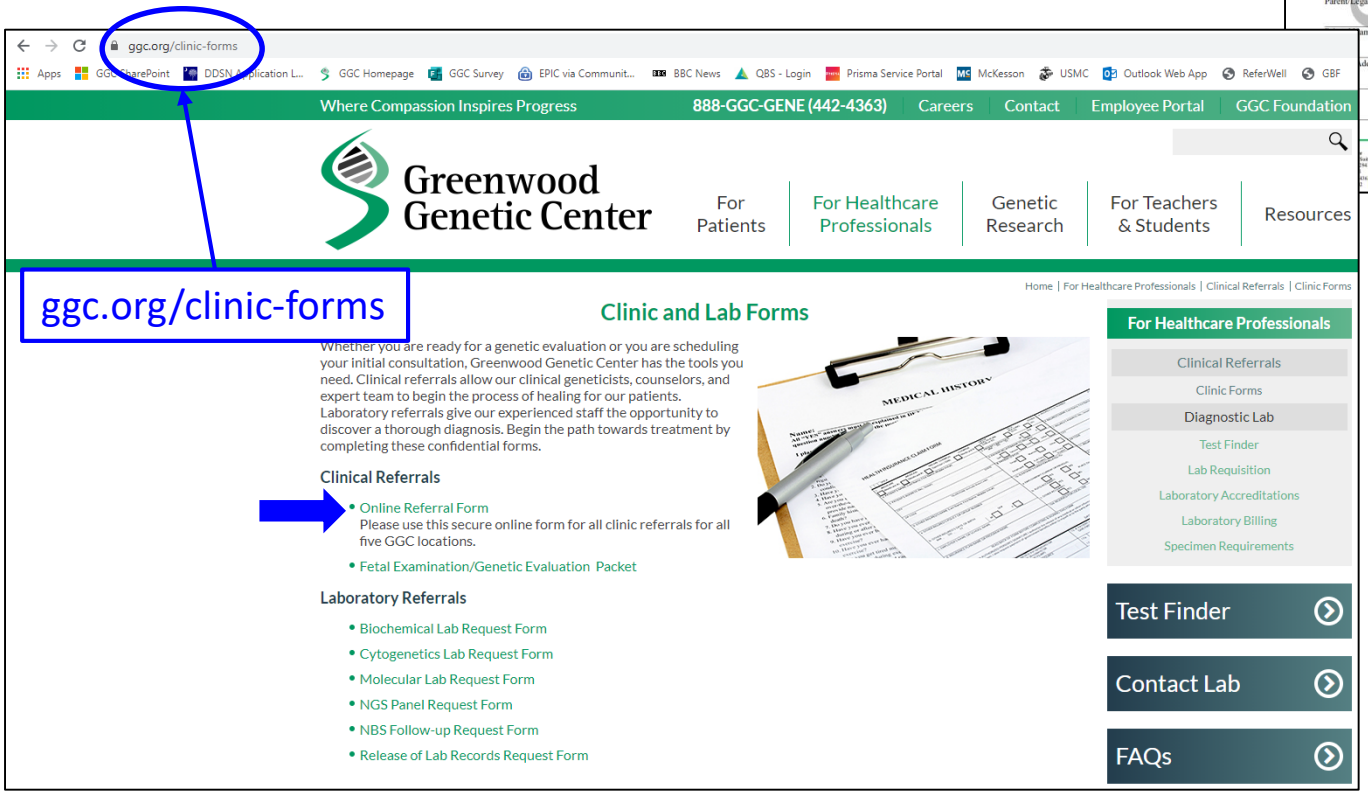
Our Referral Process

- You can place referrals into GGC via:
  - Prisma's EPIC
  - Our on-line form
- Once received, 'triaged' by genetic counselor: urgent, routine, denied





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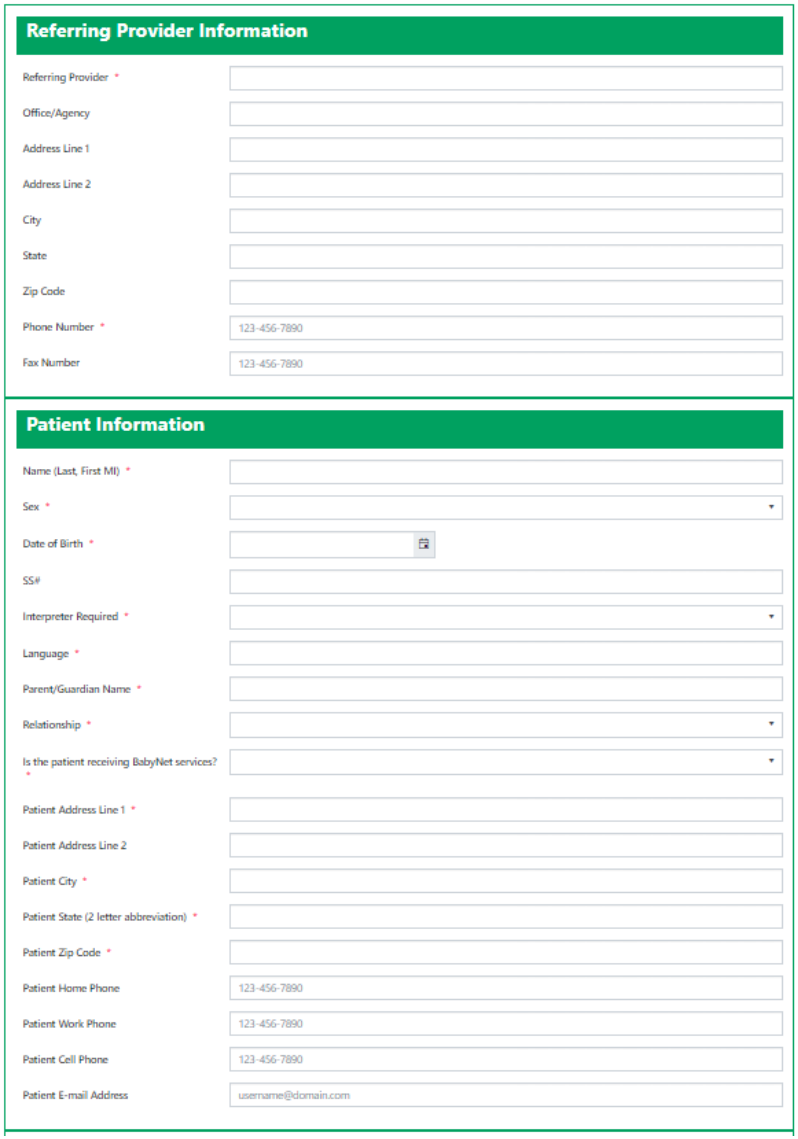
Our Referral Process (cont.)

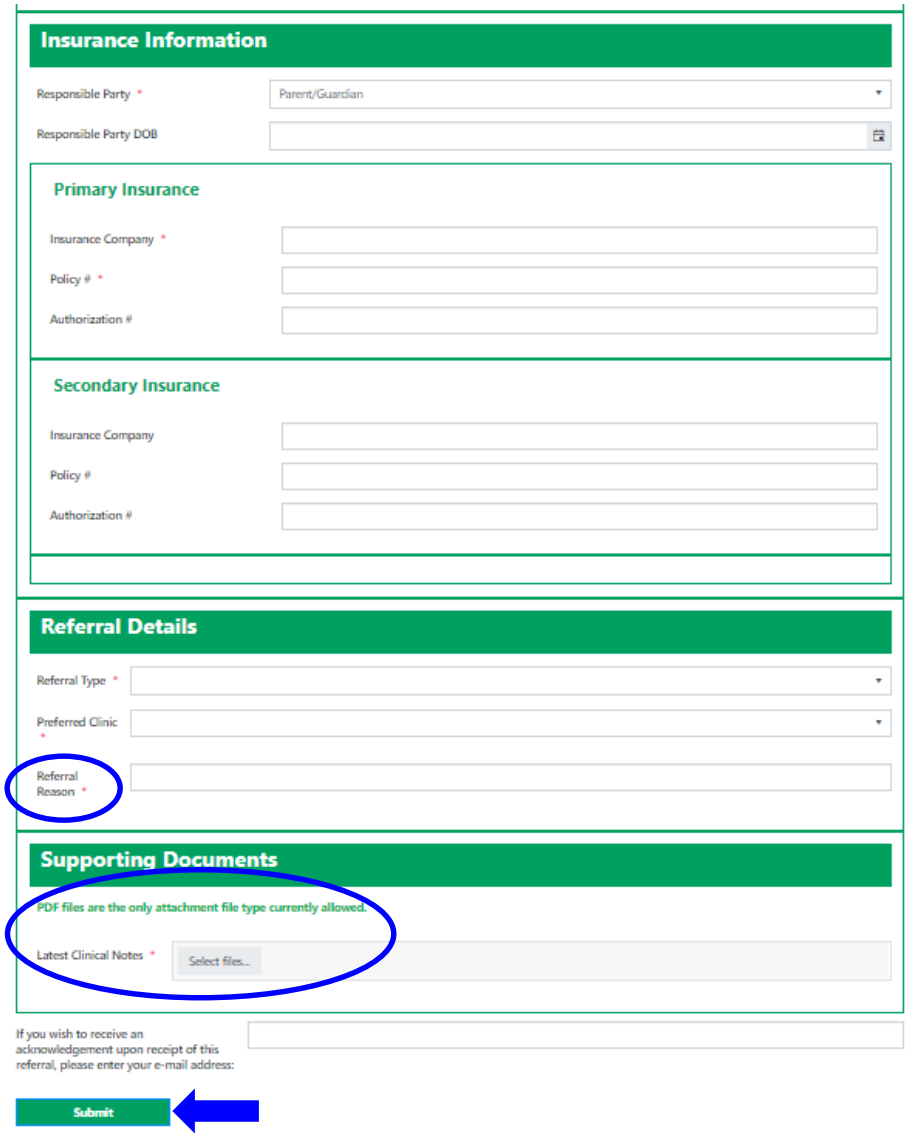


Referring Provider Information

Referring Provider *
Office/Agency
Address Line 1
Address Line 2
City
State
Zip Code
Phone Number * 123-456-7890
Fax Number 123-456-7890

Patient Information

Name (Last, First MI) *
Sex *
Date of Birth *
SS#
Interpreter Required *
Language *
Parent/Guardian Name *
Relationship *
Is the patient receiving BabyNet services? *
Patient Address Line 1 *
Patient Address Line 2
Patient City *
Patient State (2 letter abbreviation) *
Patient Zip Code *
Patient Home Phone 123-456-7890
Patient Work Phone 123-456-7890
Patient Cell Phone 123-456-7890
Patient E-mail Address username@domain.com



Insurance Information

Responsible Party * Parent/Guardian
Responsible Party DOB

Primary Insurance

Insurance Company *
Policy # *
Authorization #

Secondary Insurance

Insurance Company
Policy #
Authorization #

Referral Details

Referral Type *
Preferred Clinic *
Referral Reason *

Supporting Documents

PDF files are the only attachment file type currently allowed.
Latest Clinical Notes * Select files...

If you wish to receive an acknowledgement upon receipt of this referral, please enter your e-mail address:

Submit

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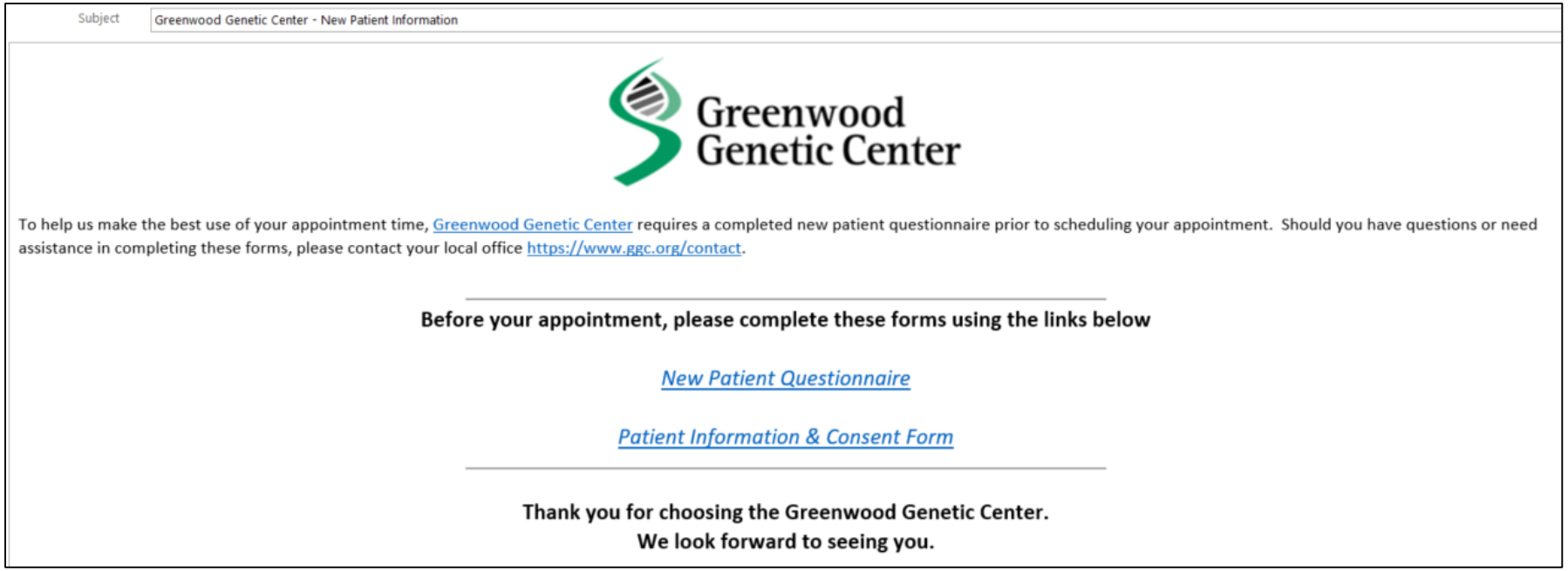
Patient Requirements

- Once a referral is validated, we reach out to the patients to:
  - Establish preferred contact info
  - Explain our patient history form
  - Explain our consent forms



Subject: Greenwood Genetic Center - New Patient Information

Greenwood Genetic Center

To help us make the best use of your appointment time, Greenwood Genetic Center requires a completed new patient questionnaire prior to scheduling your appointment. Should you have questions or need assistance in completing these forms, please contact your local office https://www.ggc.org/contact.

Before your appointment, please complete these forms using the links below

New Patient Questionnaire

Patient Information & Consent Form

Thank you for choosing the Greenwood Genetic Center.
We look forward to seeing you.

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What to Expect from a Genetic Evaluation

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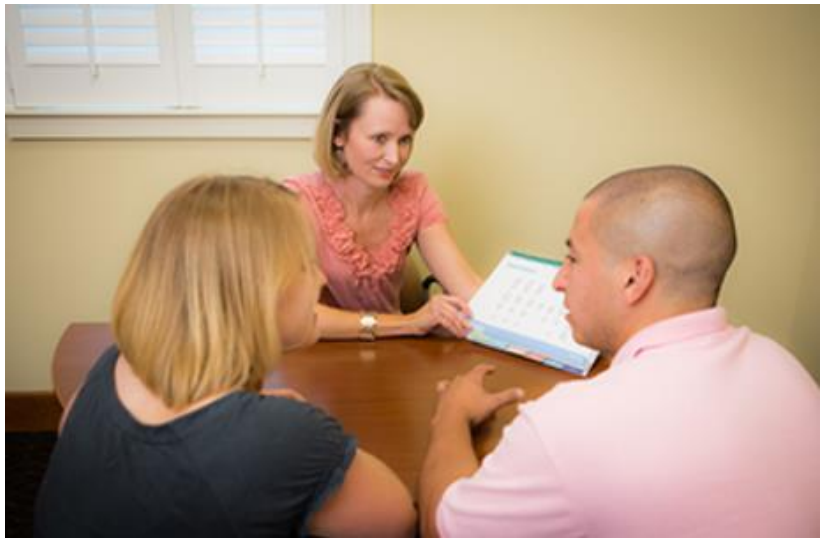
Common Indications For Genetic Referral

- Developmental delay
- Intellectual disability
- Autism spectrum disorder
- Birth defects
- Vision loss
- Hearing loss
- Growth concerns
- Metabolic condition
- Known or suspected genetic conditions



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Purpose Of Genetic Evaluation

Determine the cause of the presenting disability

- Prognosis
- Medical management, treatment
- Recurrence risk
- Support/resources for family
- End the diagnostic odyssey

Before The Genetic Evaluation

GGC reviews medical records accompanying referral and patient history form

Medical records

- Sent by SC/EI
- Referral indication
- Information re diagnosis of ID/dd/autism
- Pertinent medical records

Patient history form

- Completed by family
- Birth
- Newborn
- Medical
- Developmental
- Family

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The Genetic Evaluation: At The Appointment

- Additional history collection
- Physical exam
- Summary and plan

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The Genetic Evaluation: At The Appointment

- Allow 45-60 minutes for appointment
- Patient and parent/caregiver meet with genetic team

Additional history collection

- Genetic counselor or genetic assistant interviews family
  - Understand their primary concerns
  - Clarify and update patient information
  - Construct three-generation family tree

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The Genetic Evaluation: At The Appointment

Physical exam

Medical geneticist or physician assistant will conduct a detailed physical exam to document the patient's physical features

- Measurements
- Head-to-toe exam
- May include photographs (with family's permission)

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The Genetic Evaluation: At The Appointment

Summary and plan

- Summary of evaluation
- Recommendation for additional action to aid in making a diagnosis
  - May include genetic testing
  - May include referral to another specialist
  - May include records review
- Timeline for follow-up

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Continued Follow-Up After Genetic Evaluation

- Visit note mailed to family
- Results disclosure of genetic testing
  - Counseling for syndrome diagnosis
- Resource for family/DDSN/medical professionals
- Follow-up appointment - if recommended

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Follow-Up Appointments

Known diagnosis

- Monitor medical problems
  - Management compliance
  - Make referrals as needed
- Provide updated syndrome information
- Address new questions and concerns from family

Unknown diagnosis

- Monitor medical problems
- Check for new symptoms to help make diagnosis
- Update family history
- Consideration of additional genetic testing as appropriate

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- Pre-COVID Visits
- Post-COVID Visits
- What to Expect During Virtual Visits
- Case Example

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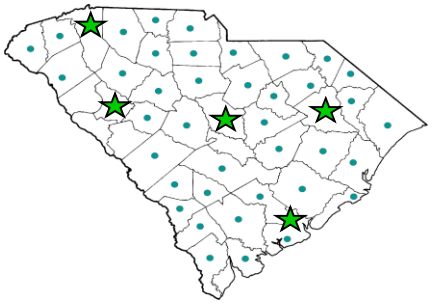
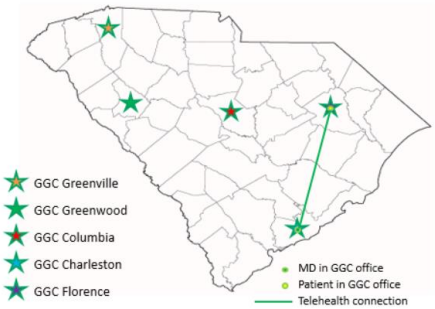
Pre-COVID Visits

- ~90% of visits were in-person
  - Patients and GGC providers present in same office
  - History, exam, sample collection done in-person
  - Requires travel
  - Relatively long wait times



- ~10% of visits were done by telemedicine
  - Patients seen at a GGC office, geneticist located at a different GGC office
  - Requires travel for patients and families
  - Somewhat shorter wait times to be seen



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Post-COVID Visits

- Transitioned patient evaluations to virtual visits
  - Patients seen in their home
  - Connect by personal computer/smartphone
    - Currently using Microsoft Teams
  - GGC providers at a GGC office or in their home
  - No travel required
  - Increased flexibility
  - Shorter wait times

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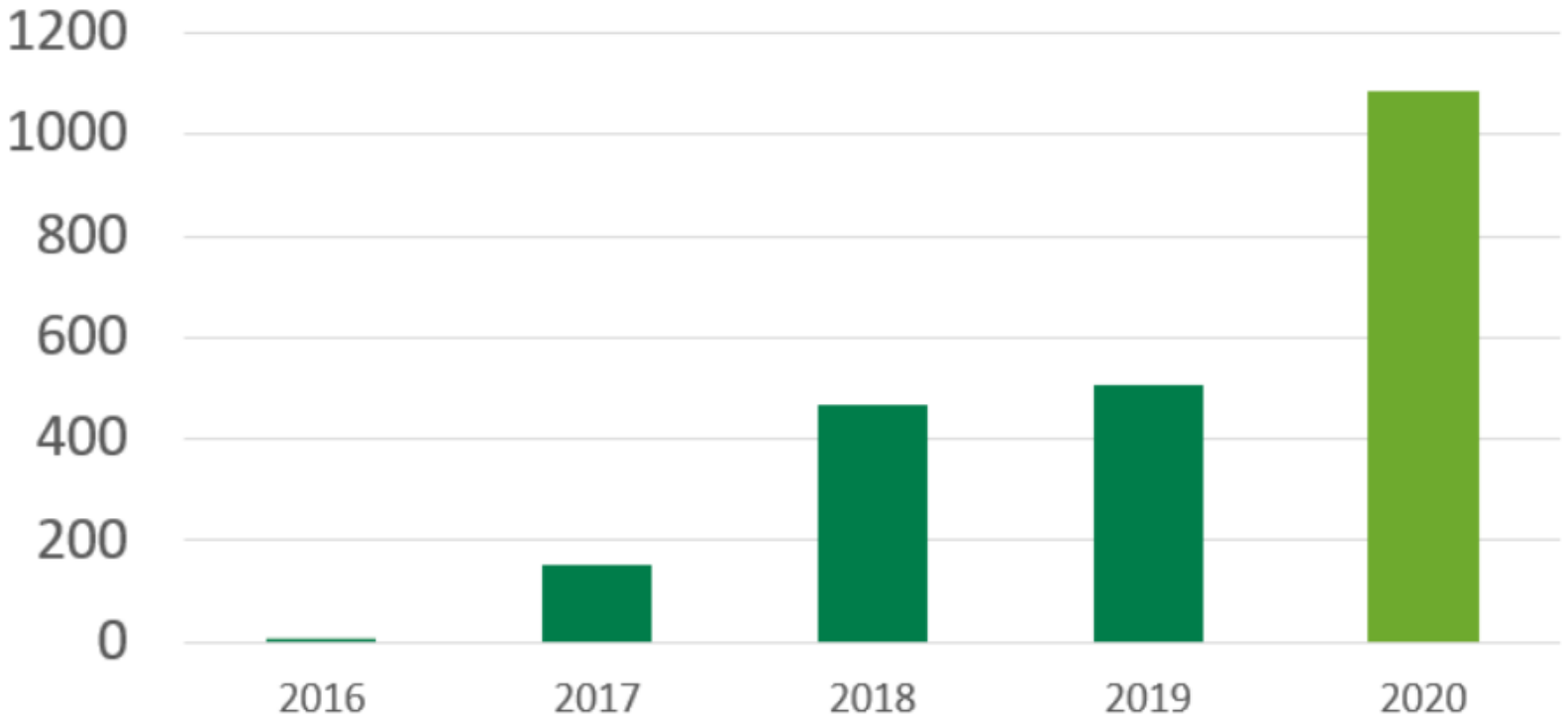
Telemedicine Clinical Visits



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What To Expect During Virtual Visits

- History Collection
  - Digital forms
- Physical Exams
  - Smartphone
- Patient Photos
  - Digital upload
- Sample Collection
  - Saliva sample

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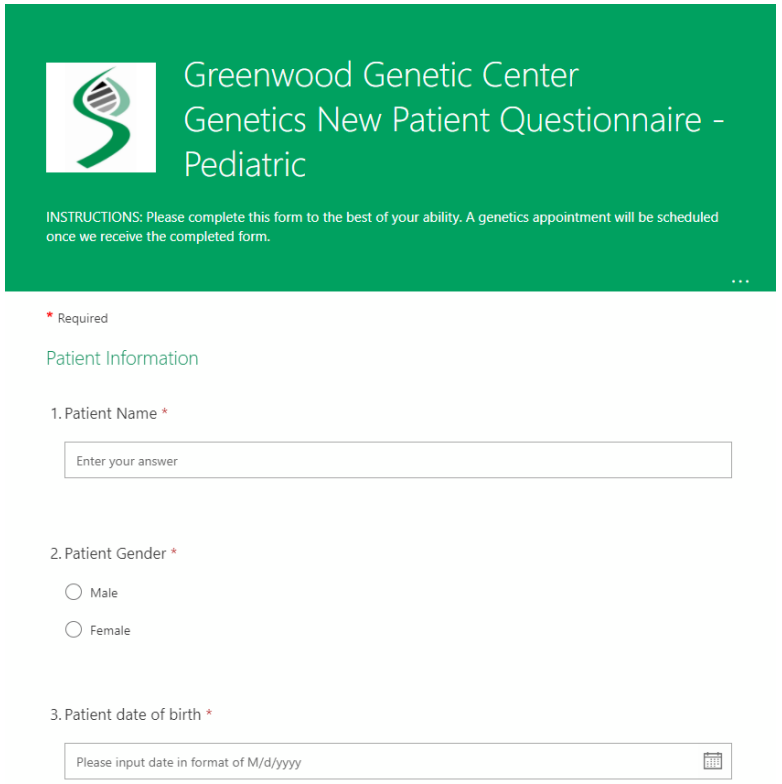
History Collection

- In March 2020, digitized consent forms and patient questionnaires
- Less time spent gathering history
- More time spent reviewing history, identifying diagnoses, and making recommendations



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Genetics New Patient Questionnaire - Pediatric

INSTRUCTIONS: Please complete this form to the best of your ability. A genetics appointment will be scheduled once we receive the completed form.

* Required

Patient Information

1. Patient Name *

Enter your answer

2. Patient Gender *

Male

Female

3. Patient date of birth *

Please input date in format of M/d/yyyy

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Physical Exams

- Telemedicine exams

  GGC telemedicine coordinator/genetic counselor facilitates exam

  - Obtains height, weight, head circumference
  - May use peripheral devices to allow geneticist to see relevant exam findings

- Virtual visit exams

  Parents/Guardians act as telemedicine coordinators

  - Can potentially measure growth or convey recent measurements
  - Use personal smartphone or other devices to allow geneticist to see relevant exam findings

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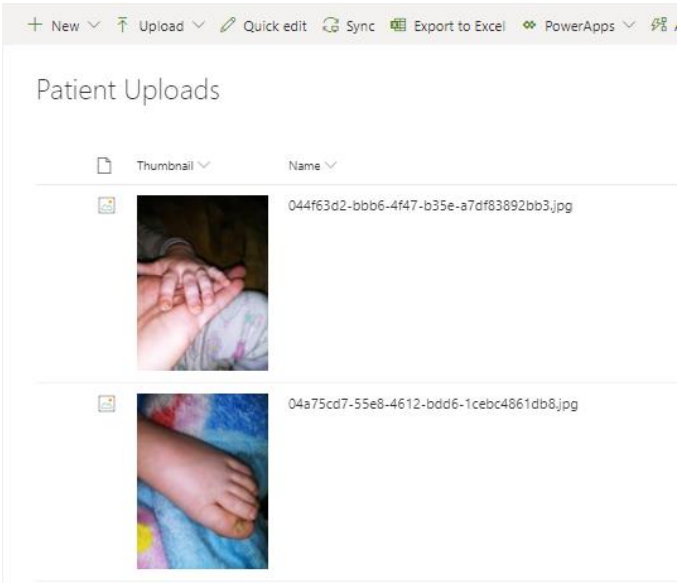
Patient Photos

- Photos typically taken in the office for in-person or telemedicine visits
- Alternative option needed to obtain patient photos during virtual visits
- Link lets families upload patient photos
  - Especially important for virtual visits which may have less detailed physical exams



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Sample Collection

- Pre-COVID

  Majority of genetic testing done by GGC providers collecting blood samples during in-person and telemedicine visits

- Post-COVID

  Majority of genetic testing done by sending saliva kits to families to collect samples

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Case Example - History

- 7 year old female referred in May 2020
  - Scheduled for virtual visit
  - Digital history form completed
    - Evaluated by orthopedics for knock knees
    - Concern for precocious puberty
    - History of multiple café-au-lait macules

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Case Example - Differential Diagnosis

- Concern for possible neurofibromatosis type 1
  - Relatively common autosomal dominant genetic condition
    - 1 in 3,000 births
  - Due to mutation in NF1 gene
    - 50% inherited
  - Associated with multiple café-au-lait macules with smooth borders (coast of California)
  - Diagnosis can be confirmed by NF1 testing of blood or saliva sample

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Case Example - Exam

- Virtual physical exam
  - Patient's mother used personal smartphone
  - Multiple, large cafe-au-lait macules with jagged, irregular borders
  - No axillary/inguinal freckling
  - Adequate exam but requested patient photo upload to further evaluate skin findings

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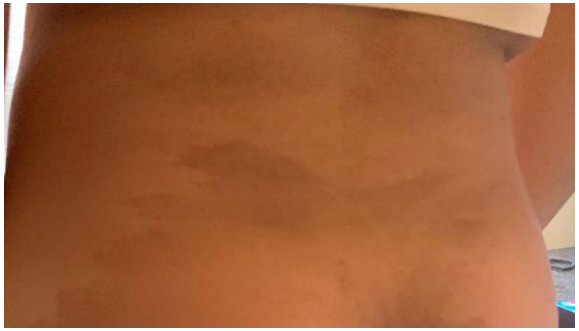
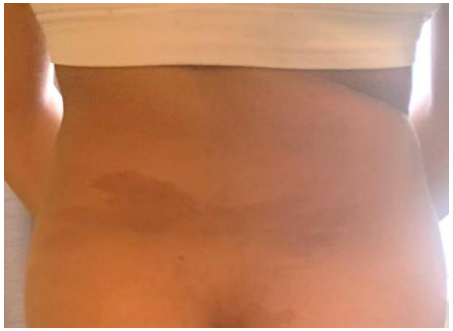
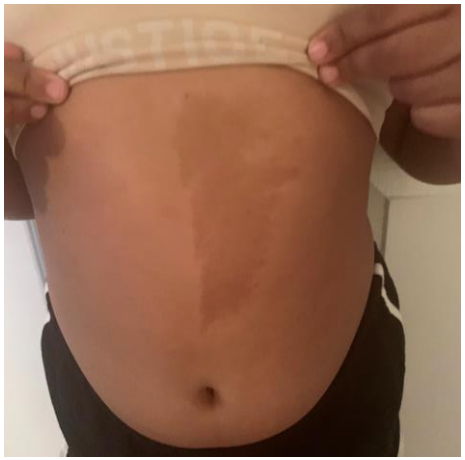
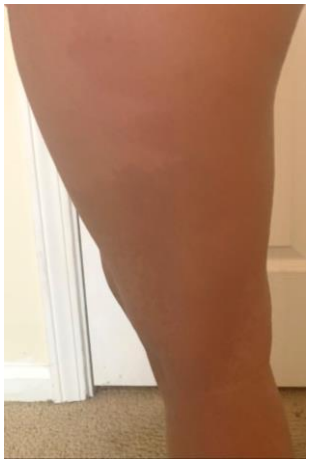
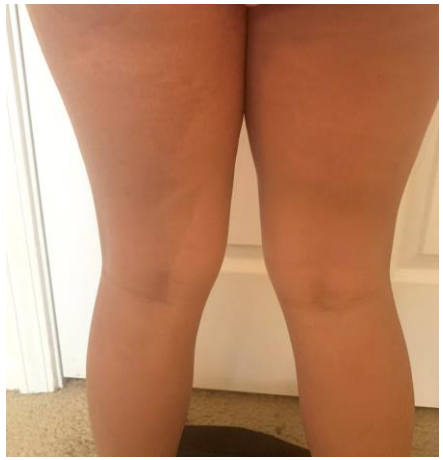
Case Example - Photo Uploads

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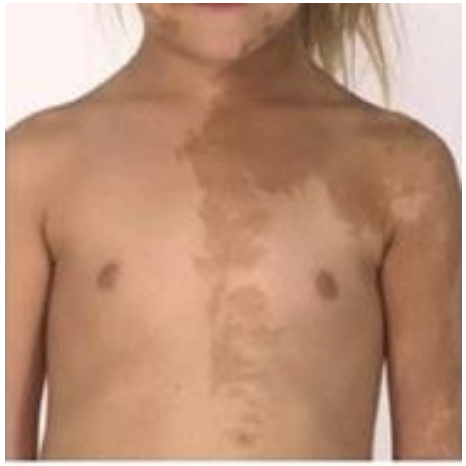
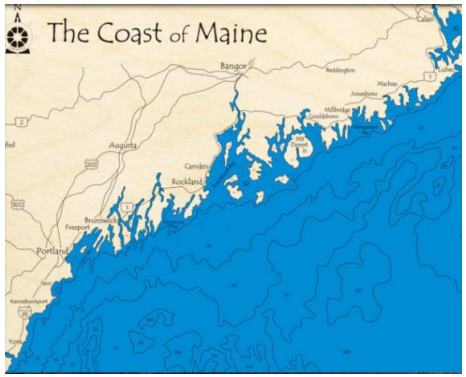
Case Example - Differential Diagnosis

- McCune-Albright syndrome
  - Rare
    - 1:100,000-1:1,000,000
  - Not inherited
    - Mosaic mutation in GNAS gene
  - Associated with multiple café-au-lait macules with jagged borders (coast of Maine)
  - Diagnosis confirmed by GNAS gene testing
    - 20-30% detection on blood or saliva
    - 80% detection on affected tissue





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Case Example - Sample Collection

- Saliva kit sent to family
  - Collected by patient's mother and returned to GGC lab for GNAS gene testing
  - GNAS result: normal
- Skin biopsy
  - In order to look for mosaicism, patient seen in-person to collect sample from affected area
  - GNAS result: pending
- Virtual visit planned to counsel family about test results and recommendations

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Genetic Testing Basics
(Chromosomes/Array/Panels/Exomes)

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Confirm a Diagnosis

Find a Diagnosis

Prove a Diagnosis

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70% of medical decisions are based on lab results

"It is fair to say that the Human Genome Project has not yet directly affected the health care of most individuals"

Francis Collins, 2010

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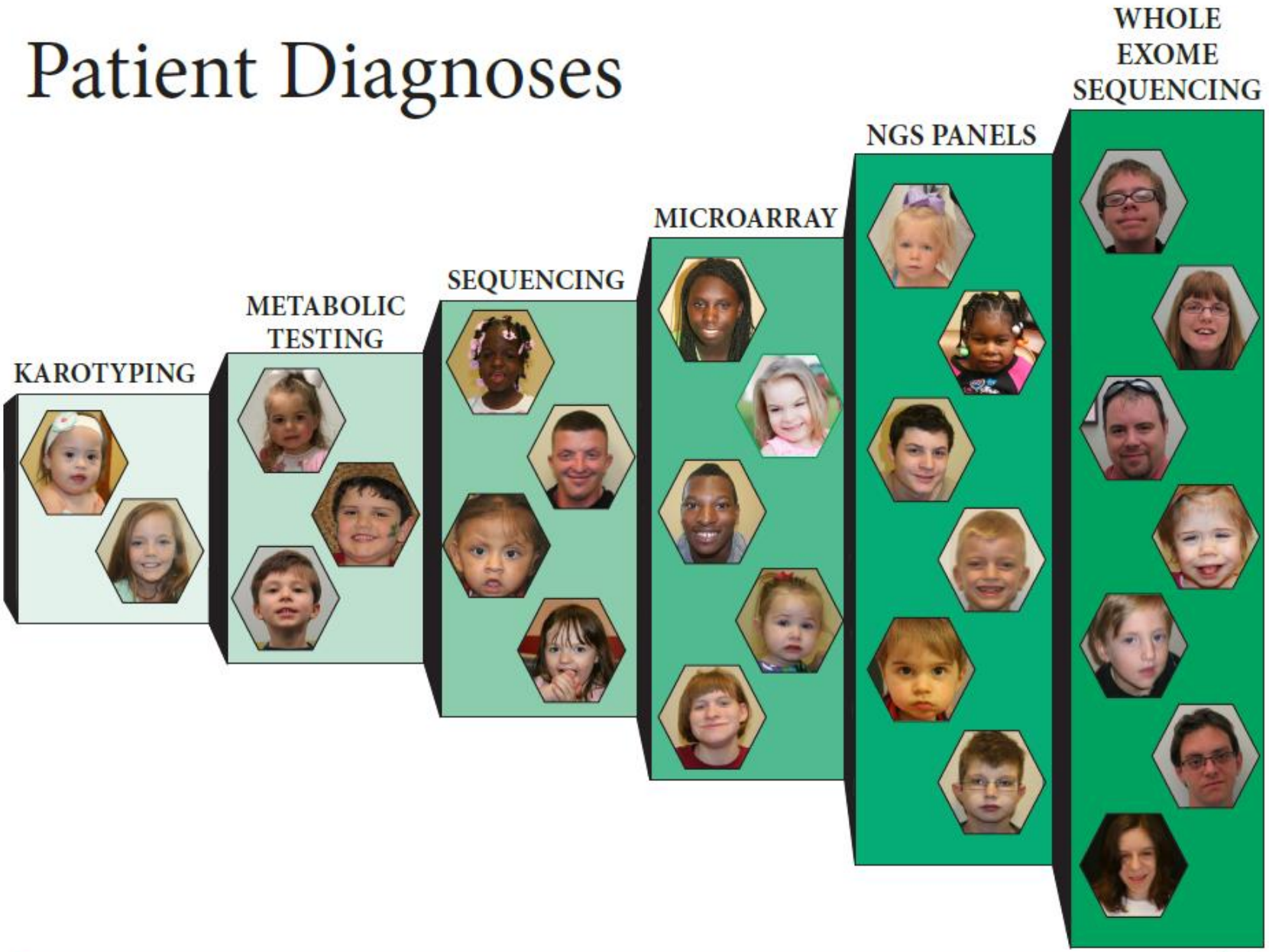
Patient Diagnoses



Diagnostic Laboratories

- Biochemical Lab
  - Metabolic studies and enzyme analysis
  - Newborn Screening support
- Cytogenetic Lab
  - Karyotyping and FISH
  - Microarray
- Molecular Diagnostic Lab
  - PCR-based testing
  - Targeted Sequencing
  - Next Generation Sequencing: exomes and genomes

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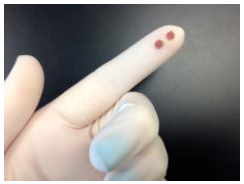
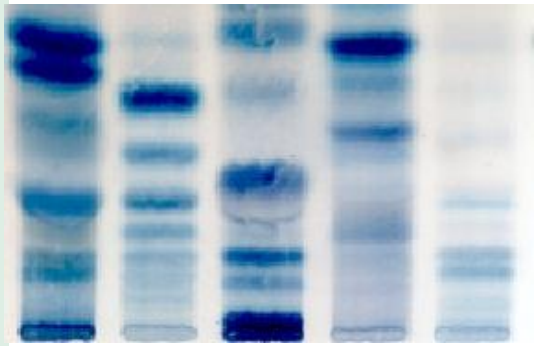
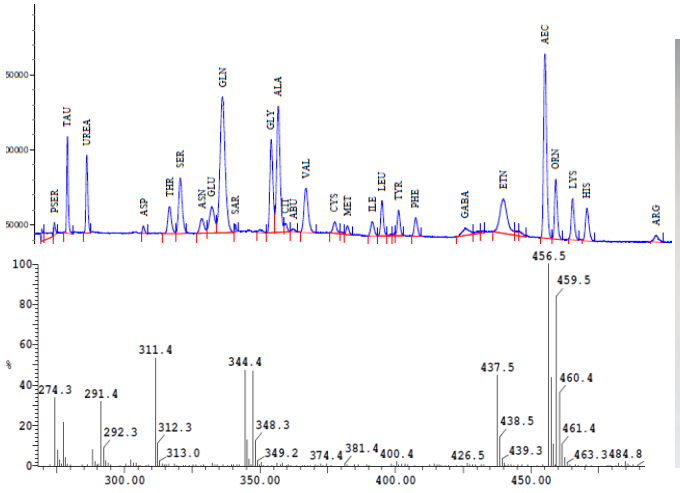


Biochemical Genetics Laboratory

- Test menu of >60 clinical tests and panels for >120 analytes
- National leader in Lysosomal Storage Disease testing
- Contracts with international pharmaceutical companies
- Newborn Screening follow up for the State of South Carolina





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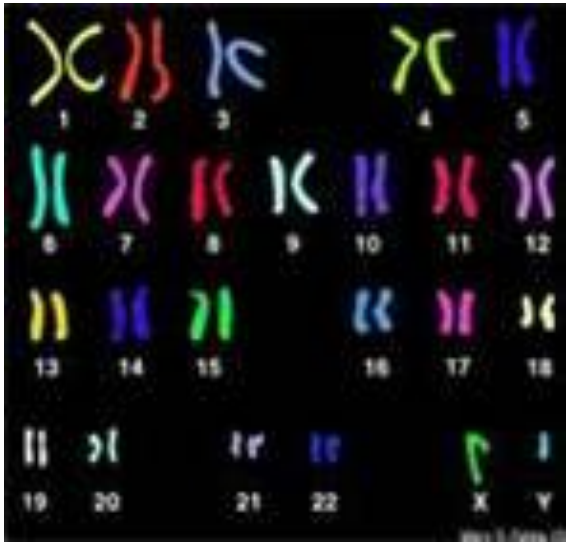
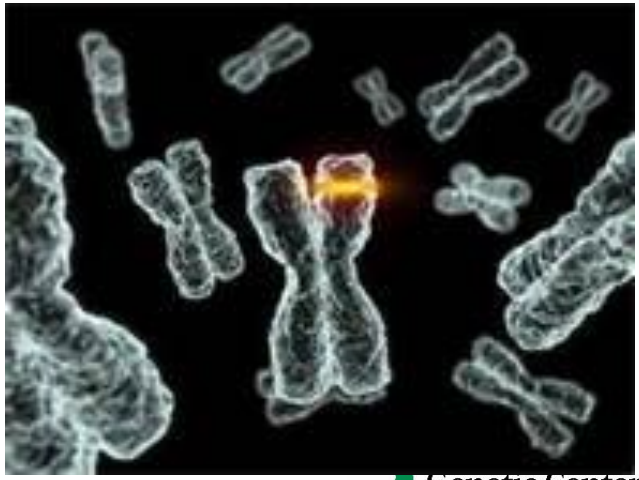
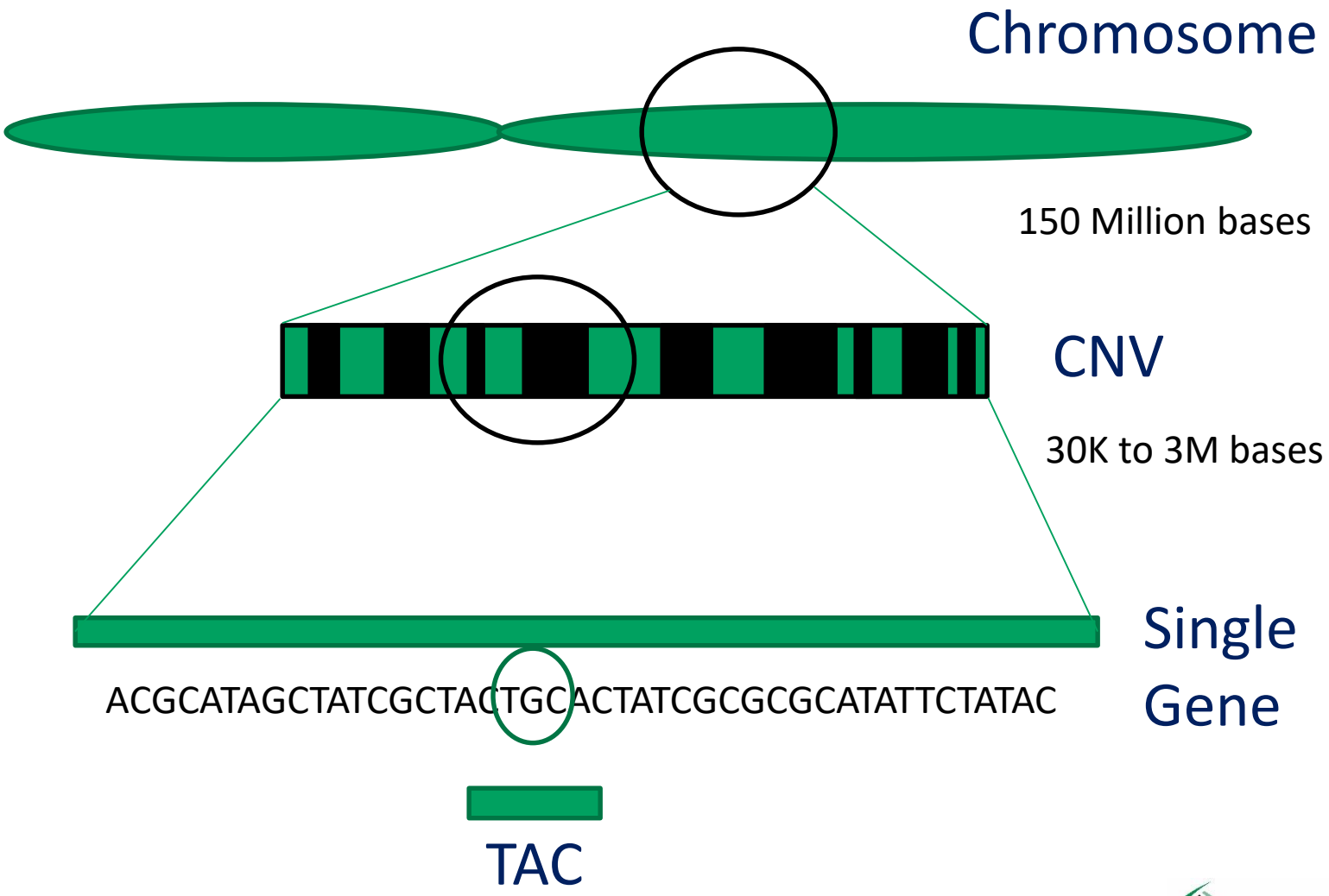
Degrees of Resolution Make the Difference





Scale of Genomic Variation



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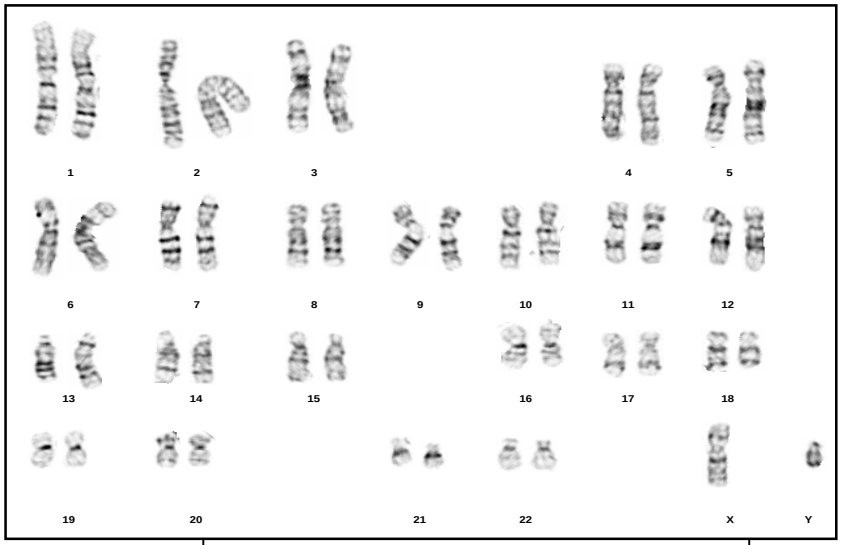
Cytogenomics Laboratory

Conventional Cytogenetics

- Karyotyping: Prenatal/Postnatal
- FISH panels: Prenatal/Oncology

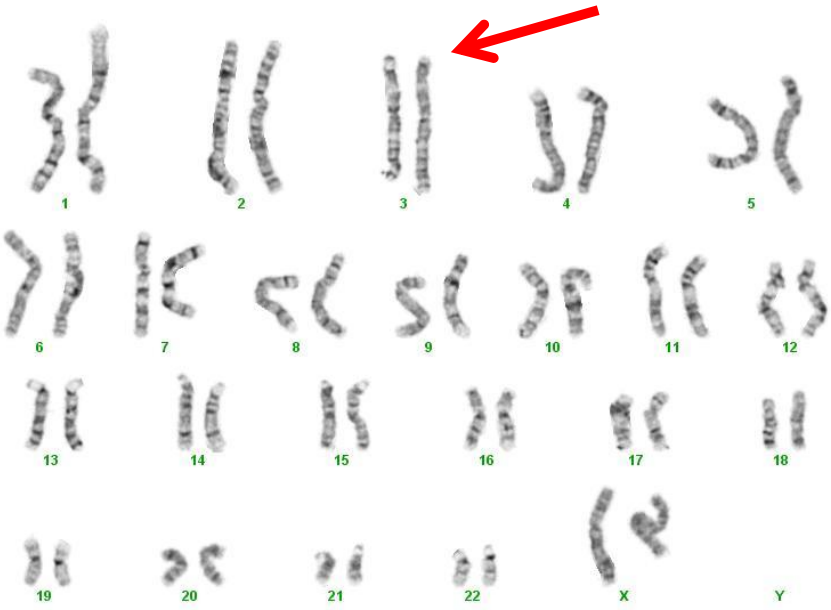


Microarray Technology

- Affymetrix CytoScan HD array

Cytogenomics Laboratory

- Global view of the genome
- Looking for abnormalities in the number or structure of chromosomes
- Aneuploidy, deletions, duplications, translocations, inversions… can cause imbalances in genes/gene products
- Samples from patients with:
  - birth defects
  - developmental problems
  - fetal anomalies
  - miscarriages
  - growth problems
  - certain cancer



46,XX,del(3)(p25)

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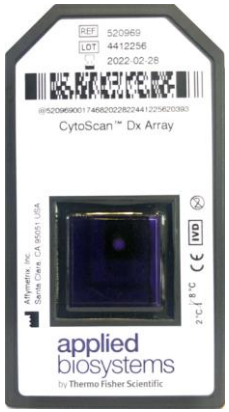
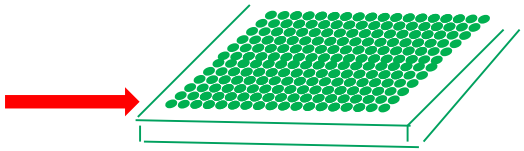
Basic Principle of SNP Microarray

Short DNA fragments can identify regions of the genome= probes

Genomic Sequence (Black)
Spaced DNA Probes (Green)

Microarray Cartridge



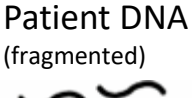


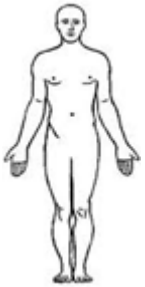
2.7 Million Probes
(multiple copies each)

Labeled Patient DNA
'Hybridizes" to the
Microarray

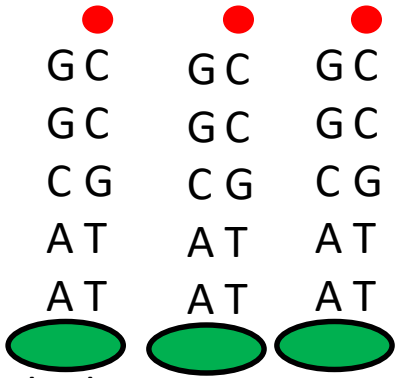
Fluorescent
Label Added

Patient DNA
(fragmented)

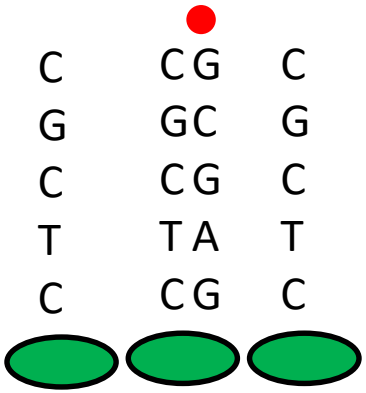




Fluorescence Intensity Correlates with Genomic Copy Number

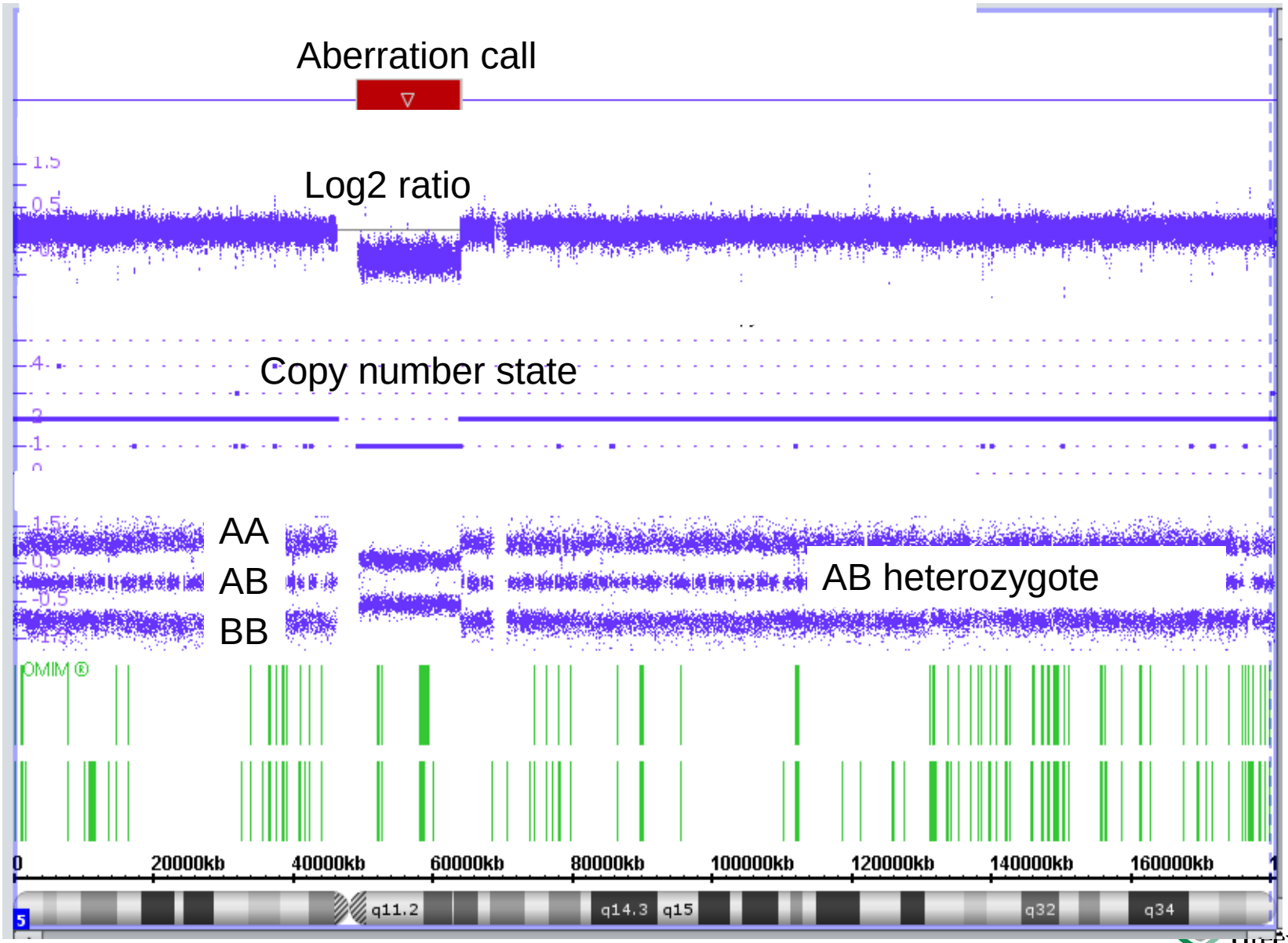


High Fluorescence= Gain



Low Fluorescence= Loss

Single copy loss on CytoScan DX



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Array Analysis

- Routinely being use for evaluation of patients with
  - Intellectual Disability,
  - Developmental Delay
  - Congenital Anomalies
  - Autism
- Platforms have different clinical sensitivity and utility due to the array design and probe coverage.
- Microarray platforms can be utilized to identify deletions/duplications and complement sequencing assays.
- More specifically, microarray testing can complement sequencing methodologies for a comprehensive analysis of recessive disorders.

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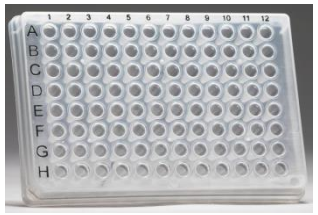
Molecular Diagnostic Laboratory

Next Generation Sequencing (NGS)

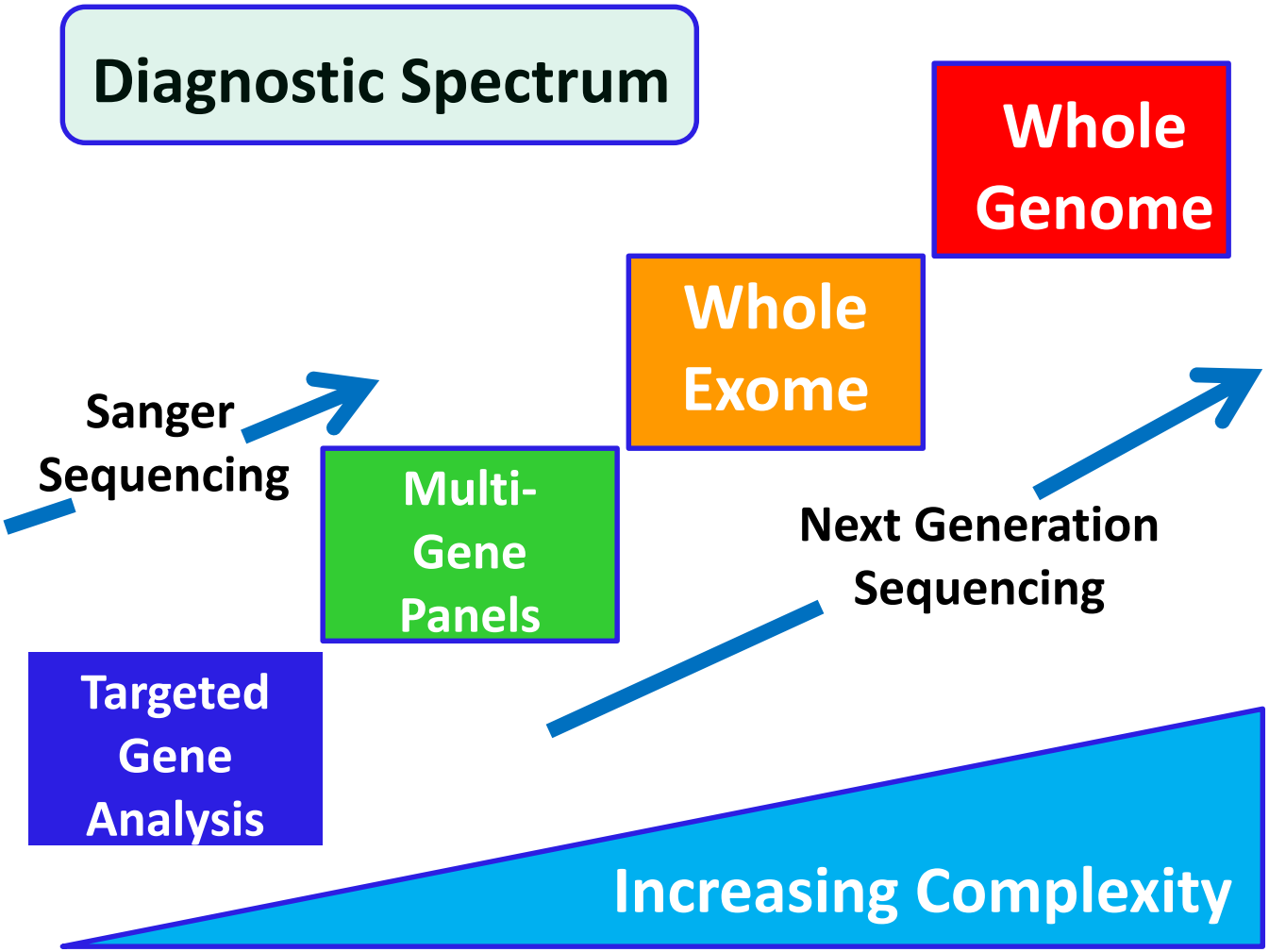
- Majority of tests involve gene sequencing (Sanger and NGS)
- NGS targeted panels
  - XLID, Autism, Epilepsy, Skeletal Dysplasia, Connective Tissue, and Lysosomal
- Whole Exome Sequencing by NGS



3730xL (Sanger):
1 gene

NextSeq500 (NGS):
100's-1000's genes

NovaSeq 6000 (NGS):
Exomes/Genomes



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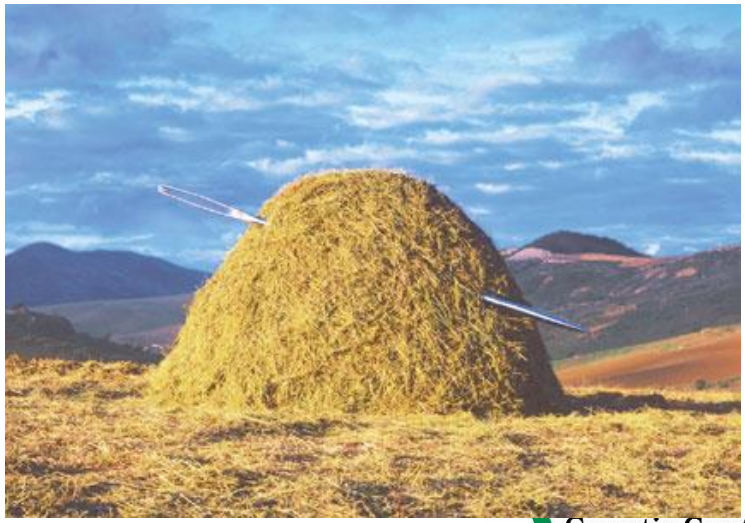
Next Generation Sequencing

- Methods that combine hardware and software tools to permit high-throughput sequence analysis of large regions of genomic DNA
- Employs nanotechnologies to reduce the size of sample components, reducing reagent costs, and enabling massively parallel sequencing reactions
- Highly multiplexed reactions allows for simultaneous analysis of millions of sequence reads
- Sophisticated computer analysis of huge amounts of information allows for detection of clinically significant variants



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The Testing Process for Next-Generation Sequencing

- Indication for testing
- Counseling
- Sequence analysis
- Communicating results/Provide counseling
- Integration into clinical decision making

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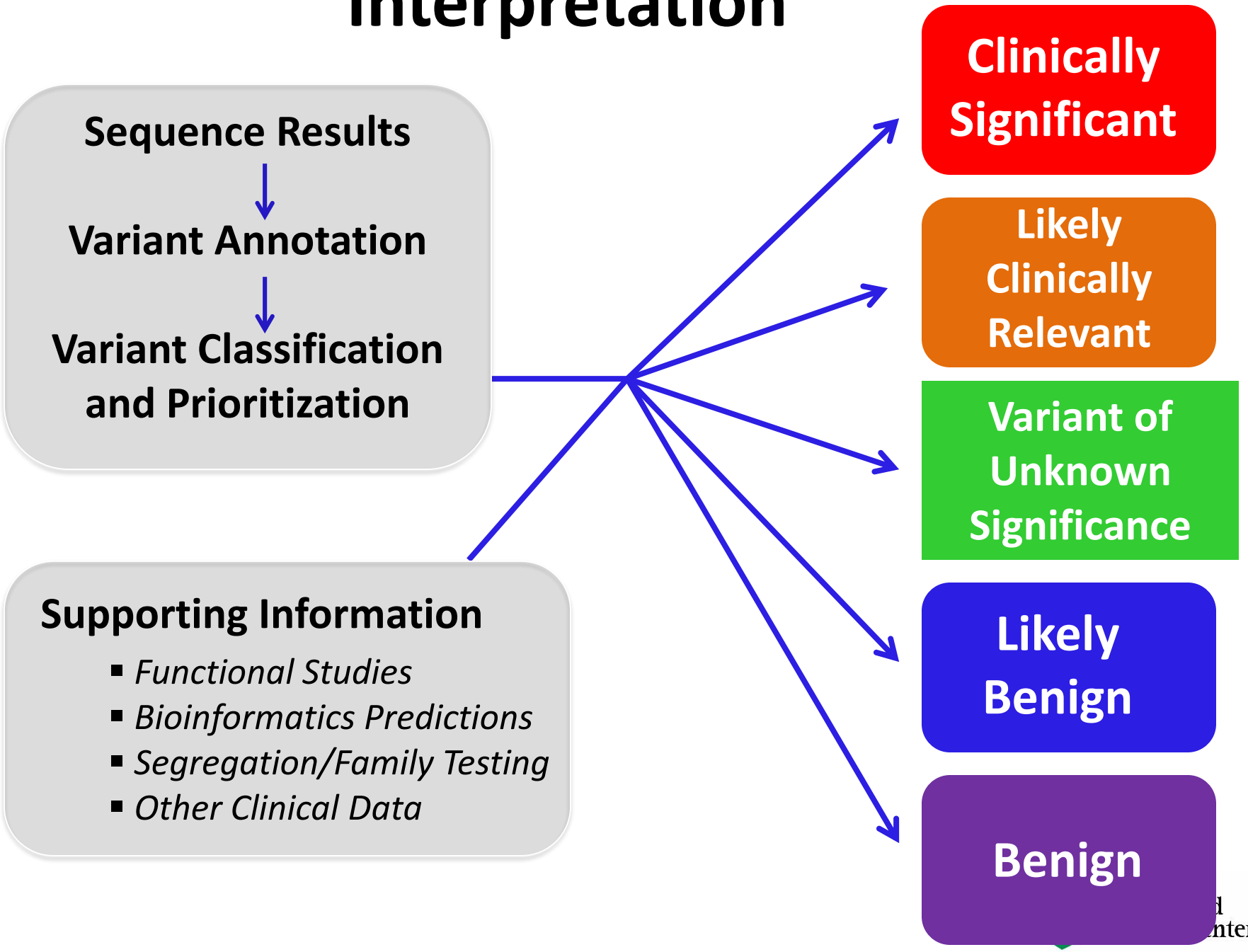
Interpretation



The Essence of Genomics

- Comprehensiveness
- Scale
- Technology development
- Rapid data release
- Social and ethical implications

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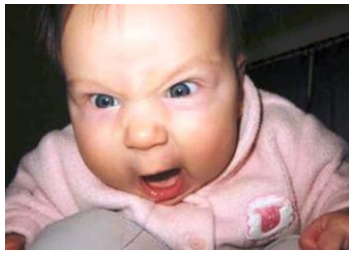
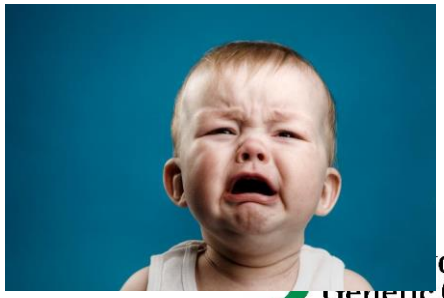
Institutional Problems

- Reimbursement
- Keeping pace with technology
- Bioinformatics and computing power
- Conducting public outreach
- Building healthcare providers' genomic competencies
- Counseling demand





EpiSign is designed to readily identify proven and reproducible epigenetic signatures by assessing genome-wide methylation. EpiSign has multiple applications in the clinical setting by providing an additional diagnostic tool beyond the current sequencing and copy number technology paradigm.

- EpiSign can also identify disease-specific methylation patterns involving multiple loci across the genome.
- These unique methylation patterns, or epigenetics signatures, have been associated with a number of single-gene disorders.

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Future Areas of Focus

- Whole Genome Sequencing
- Additional methylation-based applications
- Other molecular platforms that capture longer sequencing reads and detection of structural defects
- New options for studying RNA (expression levels)
- Metabolomics/Proteomics
- More machine learning/AI approaches to data

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Summary

- History, exam, photos and sample collection remain critical components to genetics evaluations
- COVID accelerated adoption of virtual visits
  - Patients at home
    - Less travel, shorter wait times
  - Families more involved with visit
    - Digital forms, smartphone exams, photo uploads, saliva sample collection
- Virtual visits able to efficiently identify diagnoses with appropriate recommendations and potential treatments
  - In-person visits still needed for some patient evaluations and preferred by some families

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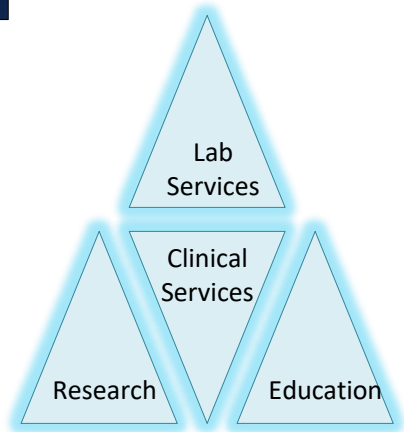
Founded in 1974 by the SC Department of Disabilities and Special Needs and the Self Family Foundation as a not-for-profit genetic institute.

Our Mission:

- ***Provide clinical genetic services***
- ***Offer a range of diagnostic testing services***
- ***Develop educational programs and materials***
- ***Conduct research in the field of medical genetics***



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