What Can GSPMC Do For Your Research in Surgery?

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Genomic Sciences and Precision Medicine Represents a Transformational Initiative for the Region

Team Science
Innovation
Research
Education
Medical Practice
Community
Industry
Consider: We had been explaining the cycle of life, health, disease, and inheritance, primarily, through the coding capacity of DNA. Thus, obtaining the whole sequence of the human genome should give us the key to understanding all these processes.
Engineering Innovations that Made the Human Genome Project Possible

Next Generation Sequencing

IT and Bioinformatics
However, we found that...
“There is a Remarkable Individual Variability in Genes, Environment, and Lifestyle for Each Person”

New World View: From not discussing, to celebrating differences, accepting that we are genetically different

https://www.broadinstitute

1000 Genomes Project Consortium
The Methodologies Developed for the Human Genome Project and the Data Derived from it Gave Rise to Other Important Complementary Disciplines
Cancer Genomics

Patients with MBC → Tumour specimen → Molecular profiling → Target identification

- L: Drug development in cohorts defined by a genomic alteration
- L: Biopsies not feasible in some patients
  - S: ctDNA
- L: High-throughput analysis not feasible in some patients
  - S: Deep sequencing, ctDNA
- L: Driver identification
  - S1: Develop cancer-related gene catalogues
  - S2: Deep sequencing, ctDNA

Targeted therapy →

- L: Availability of optimal treatment
- S: Develop precision medicine only in the context of drug access programs

Natura Reviews | Clinical Oncology
Clinomics

Clinic

Pre-test appointment
- Medical history review
- Family history evaluation
- Physical exam
- Genetic counseling session
- Insurance considerations

Patient

Indications
- Diagnostic
- Family history of possible genetic disease*
- Screening for genetic predisposition to disease or pharmacogenomics*
*Not routine clinical practice

Applications
- Modified treatment
- Personalized disease surveillance
- Familial contextualization

Informatics
- Sequence alignment
- Variant calling
- Variant filtering

Lab

Sequencing

Variant classification
- Gene – phenotype association
- Variant analysis

Clinical genomic sequencing

CLINIC AND HEALTH CARE SYSTEM

Post-test follow-up
- Medical decision making
- Re-phenotyping
- Familial segregation testing
- Input for decision support tools

Feedback to lab
- New phenotypic data
- Segregation study results

Pharmacogenomics

Goal: Determining the Right Drug at the Right Dose at the Right Time for Each and Every Patient

http://www.genesisgenome.com/images/disease_diagnosis.jpg

Epigenomics

Form of Inheritance Used by Individual Cells and Whole Organisms that Is Independent of the Coding Capacity of the DNA
Environmental Signals Acting on Cells and Whole Organisms Chemically Mark DNA, RNA, and Surrounding Proteins to Change Gene Expression and Thereby Define Normal or Diseases Phenotypes

Signals Mark DNA and Chromatin to Turn Genes On and Off at the Right Place and Time
Physiological or Pathological Stimuli Chemically Modify (Mark) the Genome and the Epigenome. These Marks are Interpreted into Define Patterns of Gene Expression that Give Rise to the Inheritable Phenotype

Marks on the DNA and Surrounding Proteins (e.g.: Histones) Signal to Induce Transitions between Euchromatin (genes on) and Heterochromatin (genes off)

Euchromatin: Active Genes

Epigenetic Marking of DNA and Histones

Heterochromatin: Inactive Genes
The Collective Group of Organisms that Form Part of the Human Microbiome

- Protects Us from Diseases
- Predisposes Us to Diseases
- Influences our Metabolism, the Circadian Rhythm of Liver Enzymes and Functions,
- Impacts other Organs (e.g. Brain)
- Modulates the Response to Many Drugs
- Can Potentially be Engineered to Fight Diseases

Addyson’s sequencing results came back. She had two separate mutations in the same gene, DGAT1. The mutations meant that the toddler was missing a critical enzyme necessary for the absorption of fats.
Functional Genomics: Basic Science Research on Disease-Associated Genomic Variants
Computational Precision Medicine and Bioinformatics

Just like Math is the Language of Physics ... Computational Biology, Informatics, and Bioinformatics are the Language of Precision Medicine
Electronic Medical Records and Wearable Personal Devices


The Combination of These Disciplines Led to the Launching of The Precision Medicine Initiative in 2015

“Tonight I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes.

And to give us all access to the personalized information we need to keep ourselves and our families healthier.”

President Barack Obama
2015 State of the Union Address | January 20, 2015
Precision Medicine

According to the White House and NIH, Precision Medicine is “an approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”

Precision Medicine was born from the convergence of both the Genomic Sciences with Bioinformatics Revolutions.

New World View: Not only are individuals different from each other, but their normal cells are different from each other, and diseases that were called the same can be different from each other.
CLARIFICATION OF TERMS

GENOMIC MEDICINE: Precision Medicine is NOT simply genomic-based medicine, but the application of NexGen is at the core of its current practice.

INDIVIDUALIZED OR PERSONALIZED MEDICINE: Although possible, it may be extremely difficult to develop a single drug for an individual:

PRECISION MEDICINE SEEKS TO...

Diagnose with Precision
Predict and Prevent with Precision
Treat Patients with Precision
Consider... Genomic Sciences and Precision Medicine as a Kuhn’s Epistemological Revolution

“The Structure of Scientific Revolutions” by Thomas Samuel Kuhn
Precision Medicine as a way of thinking... as a world view

Science is not a steady, cumulative acquisition of knowledge but rather "a series of peaceful interludes punctuated by intellectually violent revolutions." After such revolutions, "one conceptual world view is replaced by another."

“The Structure of Scientific Revolutions” by Thomas Samuel Kuhn
Paradigm Birth, Shattering and Replacement

Antiquity Greece Rome Renaissance

- Biological Revolution in Philosophy
  - Aristotle, Hippocrates-Galen

Enlightenment to XX Century

- Scientific Revolution
  - LABORATORY AND EXPERIMENTAL

80's to now

- OMICS-Computational Sciences-Technology
  - ADVANCED TECHNOLOGY
2015: A Message from the White House

https://www.youtube.com/watch?v=uOyNN0v6goE
In 2016, MCW Decided to Launch HMGC as a Comprehensive Center for Supporting a Robust Genomic Sciences and Precision Medicine Initiative in the Region Based on Continued Innovation that Supports Research, Education, and Medical Practice, as well as Community Wellness.
Role of HMGC in Genomics Sciences and Precision Medicine (GSPMC)

-To Advance **basic, translational, and clinical research** as well as the **medical practice** through innovative concepts and methodologies for **Precision Medicine** including Cancer Genomics, Clinomics, Pharmacogenomics, Epigenomics, Microbiome, Molecular Pathology, Rare Undiagnosed Diseases, Bioinformatics, System Biology, and Data Analytics.

-To Educate a **new generation** of scientists, members of medical teams, and the community in the area of Genomics Sciences, Bioinformatics, Data Analytics, and Precision Medicine

-To achieve these goals with commitment to both innovation and service
Operational Structure for a Precision Medicine Initiative

Precision Medicine Working Group

HMGC as a Genomics Sciences and Precision Medicine Support Center (GSPMC)

Cancer Precision Medicine

Clinomics Precision Medicine

Rare and Undiagnosed Diseases

Community Outreach

Planning, Evaluation and Implementation; Provides Assistance with Administrative, Legal, Communication, and Development Issues of the Initiative

Planning, Evaluation and Implementation of Scientific, Educational, and Tool Development for Precision Medicine

Implementation Level
Center Leadership

Dr. Lane  Dr. Horowitz  Dr. Silverstein  Dr. Dwinell  Dr. Basel
Epigenomics  Cancer Genomics  Clinical Genomics  Education  Rare Diseases

Dr. Kirby  Dr. Broeckel  Ms. Garman  Dr. MacKinnon  Dr. Urrutia
Microbiome  Pharmacogenomics  Administration  Molecular Pathology  Director

Bioinformatics and Systems Biology
Methodologies: For Basic Science, Clinical Research, and Precision Medicine

Cancer, Non-Cancer Clinical, and Rare Disease Genomics: Exon Panels, WES, WGS

Epigenomics:
- a-DNA Methylation: 5-C, HO, Formyl, Carbomyl Methylation
- b-ChIP-Seq: Histone Marks, Transcription Factors, Writers, Readers, and Erasers of the Histone Code
- c-RNA Modifications
- d-Nucleosome Positioning
- e-ATAC Sequencing

Pharmacogenomic Panels and Gene Network Modeling for Drug Responses

Microbiome: 16 S Sequencing and Long Read (PacBio Sequencing)

RNA-Seq

Bioinformatic Services: 1st, 2nd, 3rd Analyses Pipelines. High Level Analyses.

Functional Genomics: Molecular Modeling, Biophysics, Biochemistry, Cell Biology, Whole Organism Models
Summary

https://www.youtube.com/watch?v=HQKFgfMO5Sw
A Genomics Sciences and Precision Medicine Initiative Is Among Us and Will Stay. Embracing This Revolution Will Transform the Biomedical Landscape of Wisconsin by Bringing Innovation to Education, Research, the Medical Practice, Industry, and Community Services.
Questions...?