How will Precision Medicine Change Research and Education in Gastroenterology?

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Financial Interest Disclosure
(over the past 24 months)

No relevant financial relationships with any commercial interests
### CanMEDS Roles Covered

<table>
<thead>
<tr>
<th>Role</th>
<th>Description</th>
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<tbody>
<tr>
<td>Medical Expert</td>
<td>(as Medical Experts, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. Medical Expert is the central physician Role in the CanMEDS Framework and defines the physician’s clinical scope of practice.)</td>
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<tr>
<td>Communicator</td>
<td>(as Communicators, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)</td>
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<tr>
<td>Collaborator</td>
<td>(as Collaborators, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)</td>
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<tr>
<td>Leader</td>
<td>(as Leaders, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)</td>
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<tr>
<td>Health Advocate</td>
<td>(as Health Advocates, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)</td>
</tr>
<tr>
<td>Scholar</td>
<td>(as Scholars, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)</td>
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<tr>
<td>Professional</td>
<td>(as Professionals, physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)</td>
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Objectives

• Review the fundamentals required for precision medicine
• Review the barriers and opportunities for precision medicine
• Describe building blocks for researchers to enable precision medicine to be realized
• Discuss how precision medicine can be incorporated into education
Inefficient Imprecision medicine
Predicting the weather??

"And now the 7-day forecast..."
Precision or Individualized Medicine

• Emerging approach for disease treatment and prevention
• takes into account individual variability in genes, environment, and lifestyle for each person.
Precision or Individualized Medicine

- Emerging approach for disease treatment and prevention
- Takes into account individual variability in genes, environment, and lifestyle for each person.

P4-predictive, preventative, personalized and participatory
The time is right for precision medicine:

• Rapid advances and decreased costs of omics technology and monitoring devices
• Information technology platforms
• Agencies are interested in more targeted approach, patient engagement in research
• Cost saving- reduce or eliminate the cost of doing large phase III trials
• Patient will be engaged in research that will benefit them, not the next generation!!
Using big data to harness predictive biomarkers
Tools for assessing biomarkers

Multimodal data generation and spectroscopic platform
- NMR spectroscopy
- Mass spectrometry
- LC-MS
- GC-MS
- CE-MS
- DI-MS
- REI-MS

Analytical data
- Spectra/biological data
- Processing and classification
- Image reconstruction (spatial data)
  - M-interval spectra
  - Coomans plots, etc.

Bioinformatics and modelling
- Statistical spectroscopy
- Expert systems
- ‘-omics’ integration
  - Data integration
  - Data visualization
  - Biological interpretation
Development of new sensors/technology to record data

Smart watch

Fitbit
Development of new sensors/technology to record data

Smart watch

Sh*tbit

Fitbit
Infrastructure

• Manage and store material, knowledge and data
• Generate
• Validate
• Refine
• Interpret
Precision medicine ecosystem
“Learning health care system”
Patient perspective

- Engagement
- Knowledge of benefits/risks of data sharing
- Improved uniform consent process
Clinician’s perspective

• Determine if “biomarker” could be relevant
• If so order the appropriate test
• Know how to interpret the results
• Consider ethics
Clinician’s perspective

• Culture shift!!
• Nonconventional clinical trials
• Ethics- data identified before symptoms or disease onset??
• Patient engagement is crucial- need to know how to do this
• Aware of rapid advances in bench to bedside
• How to access networks
Researchers perspective

- Rapid translation from bench to bedside
- Experts in big data
- High quality of methods for identifying and validating biomarkers
- Functional relevance
- Develop novel sensors
Researchers perspective

• Information technology
• Networks
• Changes in clinical trial design
Basket trials

Tumour type A (lung cancer)
Tumour type B (gastric cancer)
Tumour type C (colon cancer)
Tumour type D (breast cancer)

Tumour molecular analysis

Biomarker 1
Drug 1

Biomarker 2
Drug 2
Umbrella trials
Adaptive trials

Tree diagram:
- Tumour type A (lung cancer)
  - Tumour molecular analysis
    - Biomarker 1
      - Drug 1
    - Biomarker 2
      - Drug 2
    - Biomarker 3
      - Drug 3
    - Biomarker 4
      - Drug 4
  - Analysis
    - Redefine study population
      - Stop study
    - Extend study to continue patient recruitment
      - Sub-study Drug 4
      - Sub-study Drug 4
N of 1 trials

Realizing precision medicine in Gastroenterology

Heterogeneous disease
→ New diagnostic test
→ Refined disease classification, according to prognostic implications
   - Subtype A
   - Subtype B
   - Subtype C
→ New targeted treatment
→ Clinical research
   - Outcomes
   - Safety
   - Cost
→ Clinical guidelines
→ Clinical implementation
→ Adoption by physicians and health systems
→ Adoption by patients
→ Adoption by payers

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Realizing precision medicine in gastroenterology

- Research capacity building is required for enabling individualized medicine
- Develop infrastructure to support precision medicine
- Incorporate basic knowledge of precision medicine within training programs
- Continuing medical education programs to translate rapid development of knowledge
The Diagnostic Approach to Monogenic Very Early Onset Inflammatory Bowel Disease

Holm H. Uhlig,1,2 Tobias Schwerd,1 Sibylle Koletzko,3 Neil Shah,4,5 Jochen Kammermeier,4 Abdul Eldadri,6,7 Jodie Ouahed,8,9 David C. Wilson,10,11 Simon P. Travis,1 Dan Turner,12 Christoph Klein,3 Scott B. Snapper,8,9 and Aleixo M. Muise,6,7 for the COLORS in IBD Study Group and NEOPIICS
I - Functional screening - genetic confirmation strategy

<table>
<thead>
<tr>
<th>Test</th>
<th>Disease group/syndrome</th>
</tr>
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<tbody>
<tr>
<td>CBC</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Neutrophil oxidative burst assay</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Immunoglobulins IgA, IgG, IgM, IgE</td>
<td>Lymphopenia</td>
</tr>
<tr>
<td>Lymphocyte subsets</td>
<td>CVID</td>
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<tr>
<td></td>
<td>Agammaglobulinemia</td>
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<tr>
<td></td>
<td>Hyper-IgM</td>
</tr>
<tr>
<td></td>
<td>Hyper-IgE</td>
</tr>
<tr>
<td>FOXP3+CD25+CD4+ T cells XIAP</td>
<td>IPEX</td>
</tr>
<tr>
<td>IL10 suppression of LPS induced PBMC activation</td>
<td>XLP2</td>
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Patient history
Family history
Establish IBD like pathology
1. Histology
2. Extent of disease
3. Disease activity
by upper- and lower-GI endoscopy and histology, imaging, biochemistry (CBC, CRP, ESR, albumin, consider fecal calprotectin)
Consider/exclude infections (such as Giardia, CMV, C difficile, TB, HIV...)
Consider/exclude other causes of intestinal inflammation such as celiac disease, allergic colitis (CMPA)

II - Genetic screening functional confirmation strategy

- Multiple candidate sequencing
- Whole exome sequencing
- Whole genome sequencing

Limited functional confirmation