Basic Science Year in Review

Nicola L. Jones, MD, FRCPC, PhD
Senior Scientist, Cell Biology
Sickkids, University of Toronto

Objectives

- *To provide an overview of recent developments in basic science that are relevant to the NASPGHAN community*
- *To apologize to the many individuals whose papers I did not have time to present*

Dr. Claude Roy

The New York Times The New York Times | http://nyti.ms/1HBidth

SundayReview | EDITORIAL

Why Science Needs Female Mice

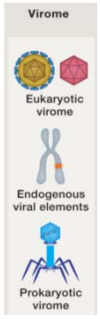
By THE EDITORIAL BOARD JULY 18, 2015

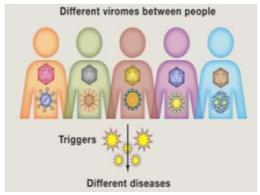
Scientific research has a gender gap, and not just among humans. In many disciplines, the animals used to study diseases and drugs are overwhelmingly male, which may significantly reduce the reliability of research and lead to drugs that won't work in half the population.

The Microbiome

- Who's there?

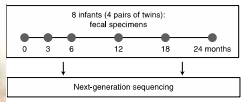
The gut microbiome goes viral!





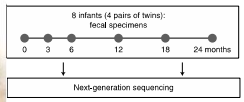
Virgin, Cell 2015

Infant gut microbiome



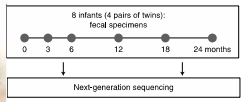
Lim et al., Nature Medicine 2015

Infant gut microbiome

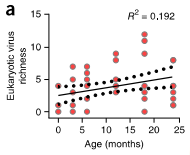


Lim et al., Nature Medicine 2015

Infant gut microbiome

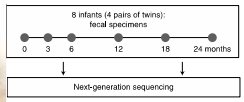


Eukaryotic virus richness increases over time

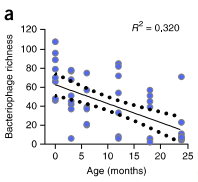


Lim et al., Nature Medicine 2015

Infant gut microbiome

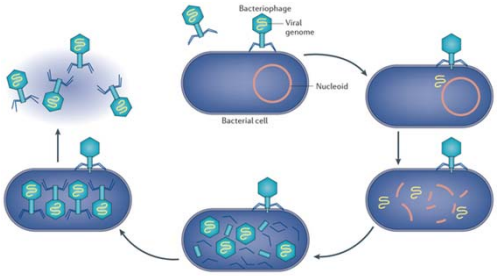


Bacteriophage richness decreases over time



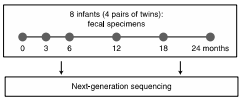
Lim et al., Nature Medicine 2015

Virome: Bacteriophages

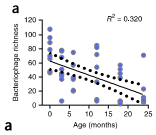


Nature Reviews | Drug Discovery

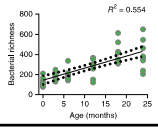
Infant gut microbiome



Bacteriophage richness decreases over time

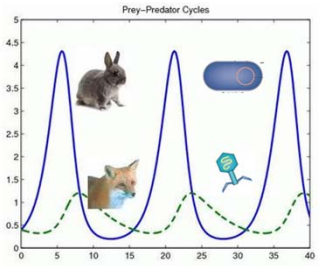


Bacterial richness increases over time

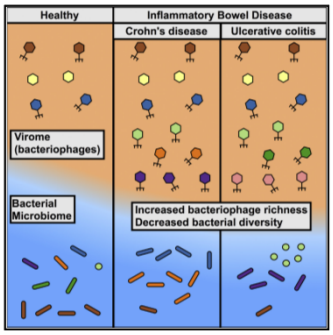


Lim et al., Nature Medicine 2015

Predator prey model

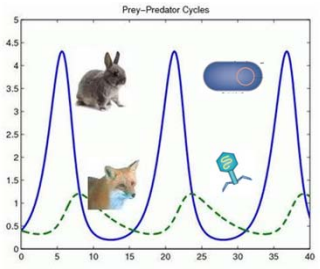


"Immature" IBD virome

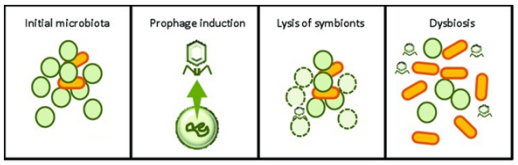


Norman et al., Cell 2015

Predator prey model

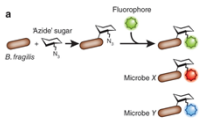


Proposed model of effects of virome on IBD dysbiosis



Norman et al., Cell 2015

The gut microbiome- real time imaging



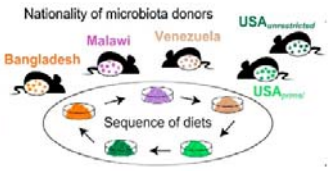
[redacted]

Geva-Zatorsky et al., Nature Medicine 2015

Microbiome to Medicine

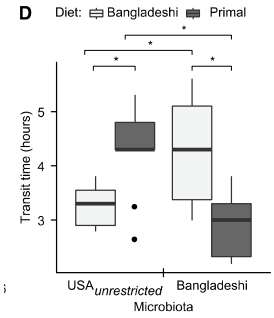
- What are they doing?

How does the microbiome and diet effect motility?



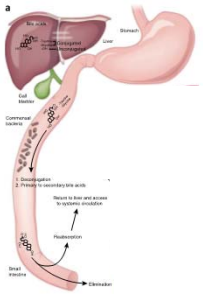
Dey et al., Cell 2015

Intestinal transit and microbiota

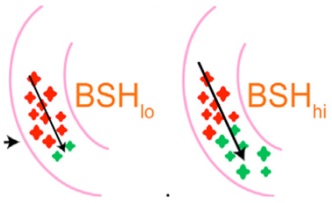


Dey et al., Cell 2015

Microbial bile salt deconjugation



Bacterial bile salt deconjugation increases motility



Dey et al., Cell 2015

The Importance of Diet

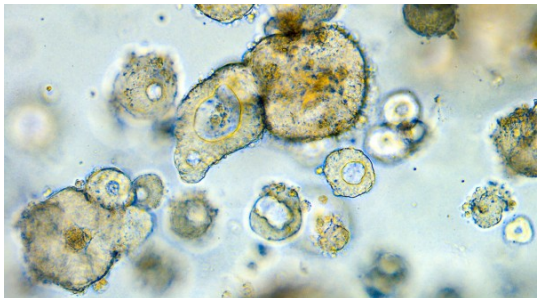
Dey et al., Cell 2015

Our Personal Microbial Cloud

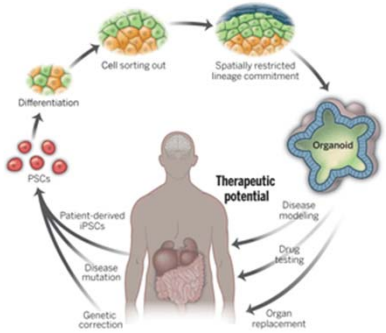
Meadow et al., PeerJ 2015

The Wearable Microbiome

Organoids going beyond culture



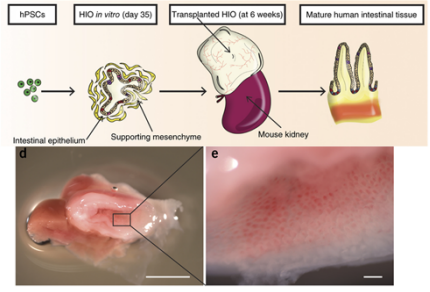
Therapeutic potential



Improving maturation and function

An *in vivo* model of human small intestine using pluripotent stem cells

Carey L Watson[1,2,10], Maxime M Mahe[1,10], Jorge Múnera[3], Jonathan C Howell[4], Nambirajan Sundaram[1], Holly M Poling[1], Jamie I Schweitzer[3], Jefferson F Vallance[2], Christopher N Mayhew[3], Ying Sun[6], Gregory Grabowski[6,7], Stacy R Finkbeiner[8], Jason R Spence[8], Noah F Shroyer[5,9], James M Wells[3] & Michael A Helmrath[1,2]

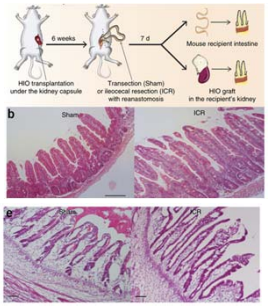


Watson et al., Nature Medicine 2014

Transplanted organoid shows adaptation

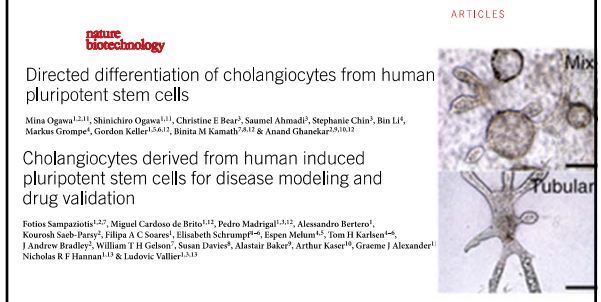
Intestine

Organoid



Watson et al., Nature Medicine 2014

Organoids: modeling disease and therapies



nature biotechnology

ARTICLES

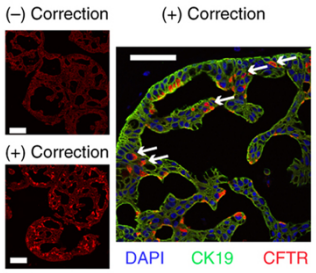
Directed differentiation of cholangiocytes from human pluripotent stem cells

Mina Ogawa[1,2,11], Shinichiro Ogawa[1,11], Christine E Bear[3], Saumel Ahmadi[3], Stephanie Chin[3], Bin Li[4], Markus Grompe[4], Gordon Keller[1,5,6,12], Binita M Kamath[7,8,12] & Anand Ghanekar[2,9,10,12]

Cholangiocytes derived from human induced pluripotent stem cells for disease modeling and drug validation

Fotios Sampaziotis[1,2,7], Miguel Cardoso de Brito[1,12], Pedro Madrigal[1,3,12], Alessandro Bertero[1], Kourosh Saeb-Parsy[2], Filipa A C Soares[1], Elisabeth Schrumpf[4–6], Espen Melum[4,5], Tom H Karlsen[4–6], J Andrew Bradley[8], William T H Gelson[7], Susan Davies[8], Alastair Baker[9], Arthur Kaser[10], Graeme J Alexander[11], Nicholas R F Hannan[1,13] & Ludovic Vallier[1,3,13]

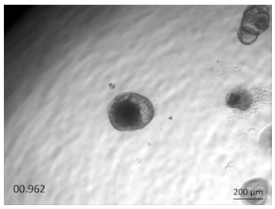
Modeling disease and therapies: CF bile duct organoids



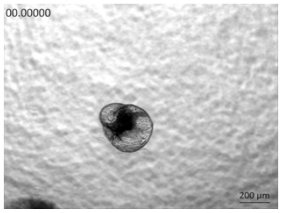
Ogawa et al., Nature Biotechnology 2015

Modeling disease and therapies

CF patient derived bile ducts

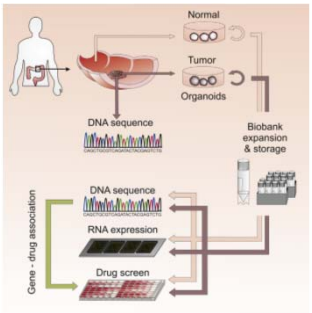


CF patient derived bile ducts plus corrector



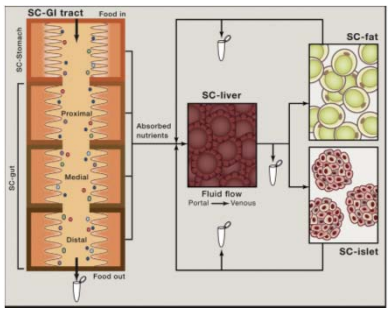
Ogawa et al., Nature Biotechnology 2015

Organoids and Personalized Therapy



van der Watering et al., Cell 2015

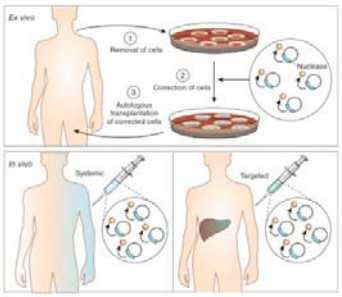
Modeling human nutrition: organoids on a chip



Ben Zvi and Melton., Cell 2015

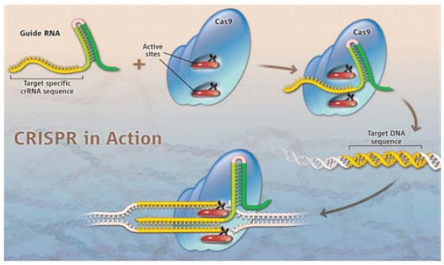
Genome editing

Genome editing- therapeutic potential

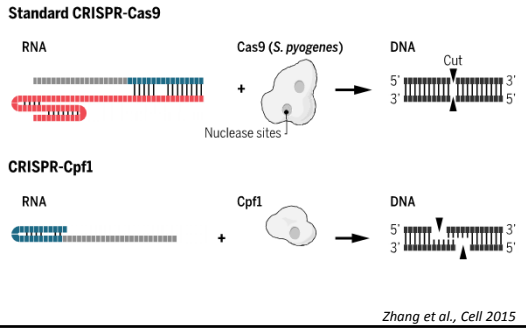


Cox et al., Nature Medicine 2015

Genome editing-CRISPR/Cas9



Improving gene editing: outsnipping Cas9



Zhang et al., Cell 2015

NATURE | NEWS

Gene-editing record smashed in pigs

Researchers modify more than 60 genes in effort to enable organ transplants into humans.

Sara Reardon

06 October 2015

Big data

ARTICLES

nature medicine

Meta-analysis of shared genetic architecture across ten pediatric autoimmune diseases

Yun R Li[1,2], Jin Li[1], Sihai D Zhao[3,43], Jonathan P Bradfield[1], Frank D Mentch[1], S Melkorka Maggadottir[1,4], Cuiping Hou[1], Debra J Abrams[1], Diana Chang[5,6], Feng Gao[5], Yiran Guo[1], Zhi Wei[7], John J Connolly[1], Christopher J Cardinale[1], Marina Bakay[1], Joseph T Glessner[1], Dong Li[1], Charlly Kao[1], Kelly A Thomas[1], Haijun Qiu[1], Rosetta M Chiavacci[1], Cecilia E Kim[1], Fengxiang Wang[1], James Snyder[1], Marylyn D Ritchie[8], Berit Flato[9], Oystein Forre[9], Lee A Denson[10], Susan D Thompson[11], Mara L Becker[12], Stephen L Guthery[13], Anna Latiano[14], Elena Perez[15], Elena Resnick[16], Richard K Russell[17], David C Wilson[18], Mark S Silverberg[19], Vito Annese[20], Benedicte A Lie[21], Marilynn Punaro[22], Marla C Dubinsky[23], Dimitri S Monos[24,25], Caterina Strisciuglio[26], Annamaria Staiano[26], Erasmo Miele[26], Subra Kugathasan[27], Justine A Ellis[28,29], Jane E Munro[30,31], Kathleen E Sullivan[4,25], Carol A Wise[32], Helen Chapel[33], Charlotte Cunningham-Rundles[16], Struan F A Grant[1,25], Jordan S Orange[34], Patrick M A Sleiman[1,25], Edward M Behrens[25,35], Anne M Griffiths[36], Jack Satsangi[37], Terri H Finkel[38], Alon Keinan[5,6], Eline T Luning Prak[39], Constantin Polychronakos[40], Robert N Baldassano[25,41], Hongzhe Li[39], Brendan J Keating[1,25] & Hakon Hakonarson[1,25,42]

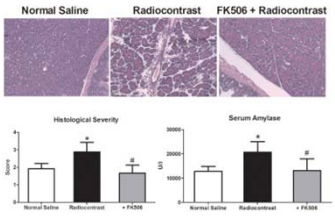
A new treatment for ERCP-induced pancreatitis?

Gastroenterology 2015;149:753–764

BASIC AND TRANSLATIONAL—PANCREAS

Exposure to Radiocontrast Agents Induces Pancreatic Inflammation by Activation of Nuclear Factor-κB, Calcium Signaling, and Calcineurin

Shunqian Jin,[1] Abrahim I. Orabi,[1] Tianming Le,[1] Tanveer A. Javed,[1] Swati Sah,[1] John F. Eisses,[1] Rita Bottino,[2] Jeffery D. Molkentin,[3] and Sohail Z. Husain[1]



The future….

- Big data meets mechanism
- Integrated team approaches
- Personalized therapy needs to consider genetics, microbiota, diet, environment…
- Microbiome to medicine