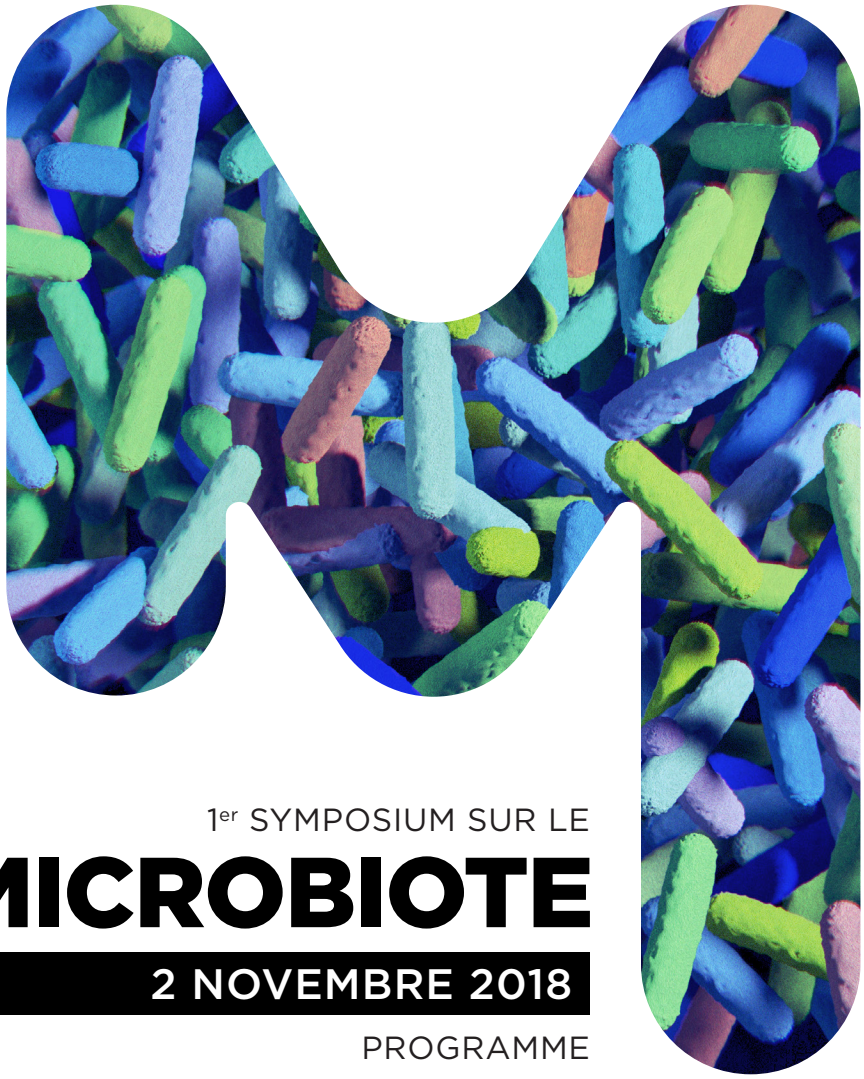


1er SYMPOSIUM SUR LE

MICROBIOTE

2 NOVEMBRE 2018

PROGRAMME

8 h à 17 h
Pavillon Roger-Gaudry
Salle K-500

LES CONFÉRENCES ABORDERONT SIX GRANDS THÈMES

- Recherche fondamentale
- Résistance contre les antibiotiques
- Maladies du système neuronal
- Cancérologie
- Maladies cardiovasculaires
- Une santé (santé animale et humaine)

Faculté de médecine
Université de Montréal et du monde.

175e

1er SYMPOSIUM SUR LE

MICROBIOTE

2 NOVEMBRE 2018

PROGRAMME

COMMANDITAIRES

Or

Bio-K+ PLUS MD

LALLEMAND

LALLEMAND HEALTH SOLUTIONS

Bronze

INSTITUTE FOR RESEARCH IN IMMUNOLOGY AND CANCER

IRIC

Université de Montréal

Prix pour concours d'affiches

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

CRCHUM

CENTRE DE RECHERCHE

Faculté de médecine

Université de Montréal et du monde.

175e

1er SYMPOSIUM SUR LE

MICROBIOTE

2 NOVEMBRE 2018

PROGRAMME

« La Faculté de médecine de l'Université de Montréal organisera son 1er symposium sur le microbiote dans le contexte des célébrations de son 175e anniversaire ».

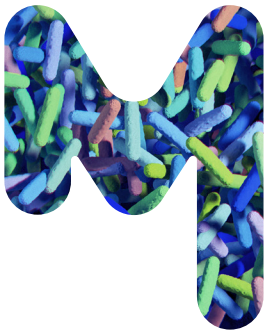
Dre Hélène Boisjoly, doyenne de la Faculté de médecine

Faculté de médecine
Université de Montréal et du monde.

1er SYMPOSIUM SUR LE

MICROBIOTE

2 NOVEMBRE 2018



PROGRAMME

8 h 00 **Inscription**

8 h 30 **Mot de bienvenue**
Marie-Josée Hébert, Vice-rectrice à la recherche à la découverte, à la création et à l'innovation
Hélène Boisjoly, Doyenne de médecine
Christian Baron, Vice-doyen à la recherche et au développement

8 h 45 **Conférencier plénier**
Your microbiome, my microbiome, our microbiome: commonalities and differences.
Jacques Corbeil, Université Laval

9 h 30 **Lessons from the analysis of plant microbiomes - a bioinformatics/ genomics approach.**
Franz Lang, Université de Montréal, Département de biochimie et médecine moléculaire

9 h 45 **The evolution of *Vibrio cholerae* within infected patients**
Jesse Shapiro, Université de Montréal, Département de sciences biologiques

10 h Pause-café (30 min)

10 h 30 **Heart-Gut-Brain axis**
Guy Rousseau et Roger Godbout, Université de Montréal, Centre de recherche du CIUSSS du Nord-de-l'Île-de-Montréal

10 h 45 **Predicting and Tuning the Course of Microbial Evolution**
Adrian Serohijos, Université de Montréal, Département de biochimie et médecine moléculaire

11 h **A synthetic biology platform to generate and screen natural product-like chemical space for novel antibiotic activities**
Almer van der Sloot (laboratoire de M. Tyers), Université de Montréal, Institut de recherche en immunologie et en cancérologie (IRIC)

11 h 15 **Detection of antibiotics and degradation products in waste waters**
Sébastien Sauvé, Université de Montréal, Département de chimie

11 h 30 **The influence of gut microbiome on cancer immunotherapy**
Bertrand Routy, Université de Montréal, CRCHUM

11 h 45 **Iron supplementation, gut microbiota, and colon carcinogenesis**
Manuela Santos, Université de Montréal, CRCHUM

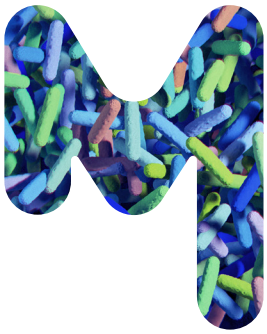
Faculté de médecine
Université de Montréal et du monde.

1er SYMPOSIUM SUR LE

MICROBIOTE

2 NOVEMBRE 2018

PROGRAMME



12 h Dîner (75 min)

13 h 15 **Conférencier plénier - Antibiotic and anticancer resistance from the environment to the human microbiome**
Gerry Wright, McMaster University

14 h **The role of the microbiome for Parkinson's disease**
Michel Desjardins, Université de Montréal, Département de pathologie et biologie cellulaire
Louis-Eric Trudeau, Université de Montréal, Département de pharmacologie et physiologie

14 h 15 **Gut Microbiota and the Gut-retina Axis in Age-Related Macular Degeneration**
Mike Sapieha, Université de Montréal, Centre de recherche de l'Hôpital Maisonneuve-Rosemont

14 h 30 Pause-café (30 min)

15 h **Microbiota of animals**
Costa Marcio, Université de Montréal, Faculté de médecine vétérinaire

15 h 15 **Pulmonary microbiome in asthma in animals**
Mathilde Leclère, Université de Montréal, Faculté de médecine vétérinaire

15 h 30 **Application of probiotics for human health**
Thomas Tompinks, Lallemand

15 h 45 **Development of a diagnostic toolbox to monitor the microbiota health in a public health laboratory**
Sandrine Moreira, Institut national de santé publique du Québec (INSPQ)

16 h **Conférencier grand public**
Yves Brun, Université de Montréal, Département de Microbiologie, infectiologie et immunologie

16 h 45 **Mot de la fin/conclusion**

17 h **Cocktail et session d'affiches**

19 h **Souper VIP (sur invitation)**

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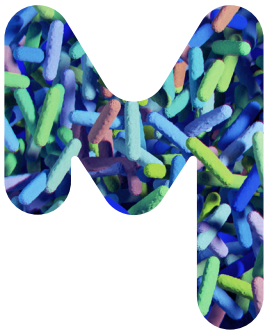
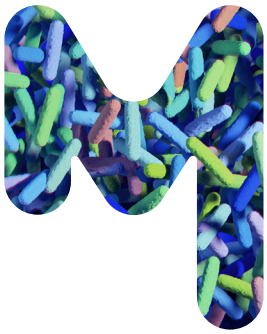


Yves Brun
Université de Montréal

The hidden world of bacteria / Le monde caché des bactéries

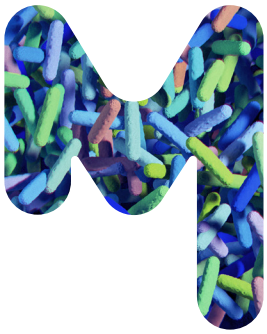
Les bactéries sont extrêmement versatiles et sont capables d'exploits remarquables. Ils sont importants pour notre bien-être en tant que membres de notre microbiote mais ils peuvent nous tuer en tant qu'agents infectieux. Ils jouent un rôle essentiel dans la fabrication de fromages au parfum délicat tel que l'Époisses mais ils sont aussi responsables de la détérioration des aliments. Ces processus collectifs sont le résultat de comportements distincts au niveau de la cellule individuelle qui gagnent à être étudiés par microscopie. Je décrirai le développement de nouveaux outils pour l'étude des bactéries par microscopie avec des exemples allant de la croissance et la morphogénèse bactérienne à la production de bioadhésifs pour l'attachement des bactéries aux surfaces lors de la formation de biofilms.



Jacques Corbeil
Université Laval

Your microbiome, my microbiome, our microbiome: commonalities and differences

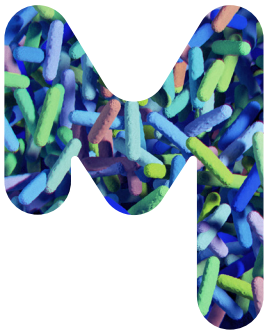
I will present an overview of the microbiome and how we handle the data; starting from assemblies to comparison of microbiomes and machine learning approaches to decipher specific phenotypes. I will also show a few examples of ongoing and future projects in my laboratory.



Marcio Costa
Université de Montréal

Microbiota of animals

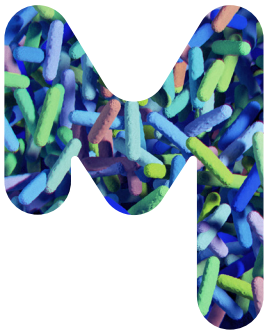
The interaction between host and their microbiome has gained enormous attention in recent years. While the majority of those studies are performed in humans and laboratory animals, several researchers are investigating the microbiota of domestic, wild and production animals. In this presentation we will donate an overview about the different studies performed at the Faculté de Médecine Vétérinaire of the University of Montreal."



Michel Desjardins et Louis-Eric Trudeau
Université de Montréal

Autoimmune mechanisms along the gut-brain axis in Parkinson's disease

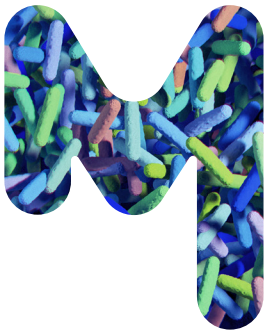
Parkinson's disease (PD) is a neurodegenerative disorder with motor symptoms linked to the loss of dopaminergic neurons (DNs). Although the mechanisms triggering the loss of DNs are unclear, mitochondrial dysfunction and inflammation are viewed as playing a key role. An early-onset form of PD affecting up to around 10% of patients is associated with mutations, including in the *PINK1* and *PRKN* (*Parkin*) genes. The recruitment of Parkin, a cytoplasmic E3 ligase, to mitochondria in a PINK1-dependent manner during cellular stress initiates the recyclingof damaged mitochondria through mitophagy. Failure to eliminate non-functional mitochondria in DNs is hypothesized to enhance oxidative stress and cause cell death. The finding that PINK1 and Parkin-independent pathways of mitophagy exist suggest that additional mechanisms driven by these proteins might contribute to PD. Evidence points to a role for innate immunity in the pathological process. PINK1 regulates the release of pro-inflammatory cytokines, while inflammation triggered by LPS injections in *Parkin* knockout (KO) mice induces DN degeneration. Furthermore, we showed that PINK1 and Parkin play a role in adaptive immunity by repressing mitochondrial antigen presentation (MitAP), suggesting that autoimmune mechanisms participate in the aetiology of PD. Here, following on the finding that LPS triggers MitAP *in vitro* and *in vivo*, we present evidence that intestinal infection with Gram-negative bacteria in Pink1 KO mice engages potentially deleterious processes involving both the innate and adaptive immune system. Infection activates MitAP and autoimmune mechanisms eliciting the establishment of cytotoxic mitochondria-specific CD8+ T cells. Remarkably, infection in these mice also leads to the emergence of severe motor impairment, reversed by L-DOPA treatment, accompanied by a sharp decrease in the density of dopaminergic axonal varicosities in the striatum. These data support the role of PINK1 as a modulator of the immune system and provide a new pathophysiological model where intestinal infection acts as a triggering event in PD, highlighting the relevance of the gut-brain axis in the disease.



Roger Godbout et Guy Rousseau
Université de Montréal

Testing the Heart-Gut-Brain Axis

Myocardial infarction (MI) can be followed by symptoms of depression in humans and we have developed a rat model. We demonstrated that the combination of the probiotics *Lactobacillus helveticus* RO052 and *Bifidobacterium longum* RO175 reduces post-MI behavioural symptoms. Our data also suggest that inflammation could be responsible for the post-MI behavioural syndrome and we hypothesize that the gut microbiota could be involved. Here we present data from young rats in which the microbiota was replaced with that of young and mature rats fed with pro-inflammatory or low-caloric diets. We show that the data indeed demonstrates an important role of the microbiota on behavior and general health possibly variations in intestinal membrane permeability.

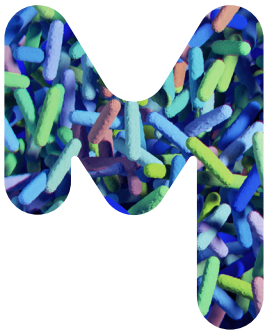


Franz Lang
Université de Montréal

Lessons from the analysis of plant microbiomes - a bioinformatics/genomics approach

The evolutionary history of eukaryotes is marked by symbiotic interactions with microbes, most notably the acquisition of an endosymbiotic α-proteobacterium about one billion years ago that has evolved into the mitochondrion. Other interactions include the acquisition of chloroplasts in green plants, and the presence of mycorrhizal fungi and rhizobacteria that colonize the plant root system from within (endophytes) or from the outside (exosymbionts, in the rhizosphere, and on aerial tissues). In the given examples the symbionts stimulate the viability, growth and health of their hosts, but there are many other instances without a benefit, or even detrimental (pathogens). In analogy to plants, animals including humans have an extraordinary rich microbiome that is located on the skin, in the mouth and the digestive tract, and in special instances microbes may penetrate into tissues. Apart from clear-cut microbial diseases, it is less well known which microbial interaction constitutes a neutral interaction, or a benefit to its host.

In our research on cranberry plants we have focused on microbial interactions that results both in healthier (disease-less) plants and higher fruit yield. To do so, we have further focused on endophytes, as the high complexity of soil microbes is most difficult to interpret. After having analyzed several hundred bacterial and fungal isolates by ribotyping (exclusion of potential pathogens) and by plant inoculation experiments, a few isolates stood out by improving plant productivity. When sequencing their genomes, it became clear that all favorite isolates had large arsenals of genes coding for biopesticides that were expressed either constitutively, or after confrontation with plant pathogens. We explain the beneficial properties of these microbes on treated plants by the suppression of microbial competitors, including pathogens, and by the production of growth-stimulating factors such as phytohormones, vitamins, and the liberation/conversion of plant-inaccessible nutrients. (Lila N. Salhi, Lise Forget, Matt Sarrasin, Gertraud Burger et B. Franz Lang)

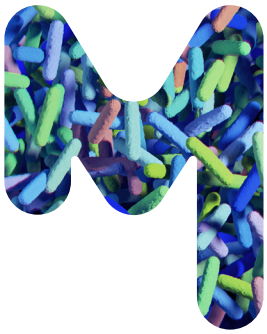


Mathilde Leclère
Université de Montréal

Pulmonary microbiome in asthma in animals

While the skin and gastrointestinal tract are well known to harbor trillions of bacteria, it was only with the development of culture-independent techniques that the lung was found to have a diverse, yet low-biomass microbiota. The role of the pulmonary microbiota is poorly defined, but there are evidences that it differs between asthmatic and healthy individuals, and that airway bacterial diversity is associated with impaired function. In many studies however, confounding factors such as environmental conditions and medication are present, and difficult to control for.

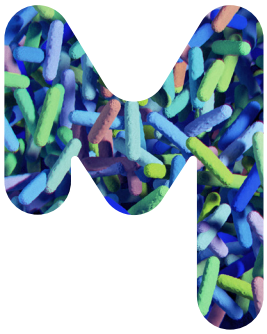
We used a naturally occurring model of neutrophilic asthma (Severe Equine Asthma, formerly "Heaves") to address this question. Six asthmatic horses receiving no medication and 6 controls were kept on pasture ("Low antigen exposure"), then housed indoors and fed good quality hay ("Moderate exposure"), and then fed poor quality hay ("High exposure"), in a cross-over design. Bronchoalveolar lavage, oral, nasal rinses and appropriate controls were collected. Sequencing of the 16S rRNA gene was done using the V4 region and Illumina MiSeq platform, then analyzed using mothur and the vegan package in R. Only horses with asthma developed airflow limitation and pulmonary inflammation with antigen exposure. Lung, oral and nasal communities were distinct from one another and clustered strongly by environmental conditions. Only the lung microbiome was different between horses with and without asthma. This study shows that the lung bacterial microbiome of healthy and asthmatic animals receiving no medication and housed together are different and vary with the antigenic exposure level.



Sandrine Moreira
INSPQ

Development of a diagnostic toolbox to monitor the microbiota health in a public health laboratory

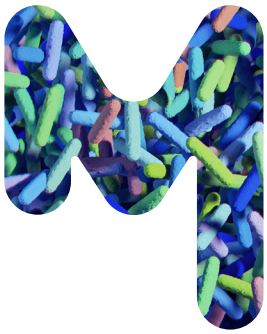
The extraordinary advancement of sequencing technologies and computing capabilities has made metagenomics accessible to clinical microbiologists in public health laboratories. Clinical metagenomics allows the characterization by new sequencing technologies of the microbial content of a clinical sample, be it a simple strain isolate or a microbial ecosystem as complex as the intestinal microbiome. Specifically, it includes methods for characterization, typing, and surveillance of pathogens as well as epidemic management. The most recent developments include universal pathogen detection that holds the promise of elucidating the 20 to 60% of diagnoses still remaining unsolved and the detection of microbiome composition imbalance (dysbiosis). Nevertheless, while these methods hold enormous potential and are widely used in research laboratories, they are still slow to be fully implemented in a clinical context. In this presentation, we will see the different use cases of metagenomics in public health, its promises, its successes and its challenges.



Bertrand Routy
Université de Montréal

The influence of gut microbiome on cancer immunotherapy

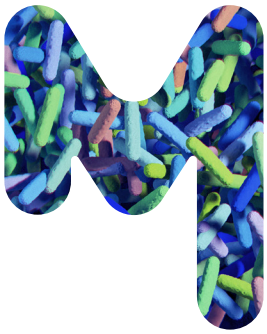
Cancer immunotherapists have been searching for biomarkers predicting patient responses to PD-1/PD-L1 blockade in neoplastic cells as well as in the immune system. An unexpected paradigm shift occurred when the composition of gut commensal microbes referred as the gut microbiome and concomitant usage of antibiotics (ATB) were associated with ICI cancer response. We showed that ATB prescription prior to or within the first month of ICI initiation negatively impacts clinical outcomes. Subsequently, we sequenced feces from advanced NSCLC amenable to anti-PD-1 mAb, and commensal bacteria Akkermansia muciniphila was found to be strongly associated with favorable tumor response. Two other groups demonstrated that melanoma patients' microbiota enriched with Ruminococcaceae and Faecalibacterium translated into a better overall response. Therefore, modification of the gut microbiome represents a novel therapeutic avenue in immuno-oncology



Manuela Santos
Université de Montréal

Iron supplementation, gut microbiota, and colon carcinogenesis

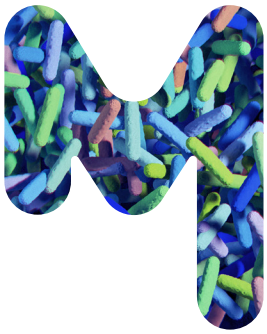
Almost all bacteria require iron for growth and survival. In order to successfully compete for this essential nutrient, bacteria developed very efficient and diverse iron uptake systems. We hypothesized that dietary iron content and iron supplementation may impact gut microbial composition. We investigated the impact of iron supplementation on the composition of the gut microbiota in the context of inflammatory bowel disease (IBD) by 16S ribosomal RNA gene sequencing. Using the dextran sodium sulphate (DSS)-induced colitis mouse model we examined the effects of iron supplementation in combination with the probiotic Escherichia coli Nissle 1917 (EcN) on colitis severity. Diets supplemented with different iron formulations had either beneficial (ferrous sulphate and ferrous bisglycinate) or detrimental (ferric EDTA and heme) effects on colitis severity depending on the type of iron supplementation used. The beneficial effect of EcN on colitis was also potentiated by oral iron supplementation. In addition, dietary heme, but not systemically delivered heme, facilitated adenoma formation in the azoxymethane/DSS colorectal cancer (CRC) mouse model. Overall, our findings suggest that the iron formulations used to treat iron deficiency may influence the gut microbiota composition and the severity of colitis. In addition, the beneficial action of probiotics in IBD may be enhanced by oral iron supplementation. Finally, our data suggest that high luminal heme levels ensuing from gastrointestinal blood losses in IBD and CRC patients may be an important contributor to gut dysbiosis.
Funding (CIHR, CCRSI and MITACS - Accelerate program)



Przemyslaw (Mike) Sapieha
Université de Montréal

Gut Microbiota and the Gut-retina Axis in Age-Related Macular Degeneration

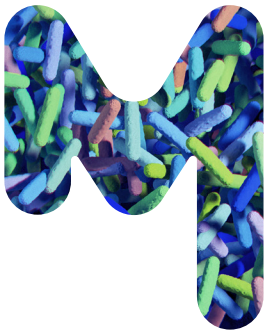
Epidemiological data suggests that in men, overall abdominal obesity is the second most important environmental risk factor after smoking for progression to late-stage neovascular (NV) AMD. To date, the mechanisms that underscore this observation remain poorly defined. In the current study, we uncoupled weight gain from confounding factors and draw a link between gut dysbiosis and choroidal neovascularisation (CNV). Using mouse models of NV AMD, microbiotal transplants and other paradigms that modify the gut microbiome, we demonstrate that gut dysbiosis leads to heighten intestinal permeability and chronic low-grade inflammation characteristic of inflammaging that ultimately exacerbates pathological choroidal angiogenesis. Our study ultimately provides evidence for gut dysbiosis and the gut-retina axis in CNV evolution.



Sébastien Sauvé
Université de Montréal

Detection of antibiotics and degradation products in waste waters

On observe des antibiotiques dans les effluents municipaux urbains ainsi que dans les analyses de lisier de porc. On a démontré la présence de résidus de d'antibiotiques de la famille des tétracyclines dans le lisier et que ces substances persistaient dans les champs et qu'elles pouvaient migrer vers les eaux de drainage qui se déversent dans les cours d'eau environnant. De plus, l'utilisation de spectrométrie de masse à haute résolution a aussi permis d'identifier et de mesurer des sous-produits de ces tétracyclines qui apparaissent souvent à des concentrations plus élevées que les molécules parentes. Par ailleurs, on a aussi identifié et confirmer la présence de substances non-ciblées, notamment la medroxyprogestérone (hormone stéroïdiennes) et la ractopamine (un beta-agoniste – d'utilisation interdite dans plusieurs pays mais pas ici). Les travaux soulignent l'importance d'évaluer le devenir environnemental des molécules utilisées ainsi que leurs produits de transformation.



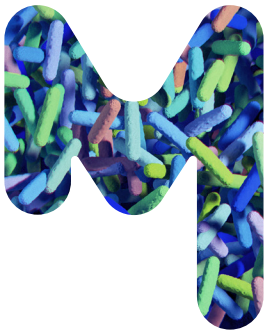
Adrian Serohijos
Université de Montréal

Predicting and Tuning the Course of Microbial Evolution

To circumvent antibiotic resistance, we need to discover new antibiotics. However, this will not be enough. We also need to conserve the efficacy and maximize the duration of usefulness of both current and future antibiotics. Antibiotic resistance will always arise, but if we are able to predict how they evolve, we can delay their emergence.

At the fundament level, the evolution of AMR, like any other biological system, is governed by processes at several scales of biological organization—molecular, cellular, organismal, and population level. Although the immediate effects of mutations are on the properties of proteins or fitness of individual cells, the eventual evolutionary success of these mutations is affected by population dynamics. In this talk, I describe our efforts to develop a quantitative and predictive model of the emergence of AMR by bridging these multiple scales in bacterial evolution.

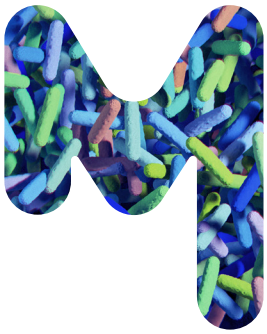
First, we determined the comprehensive “mutational landscape” of gene targets that are crucial targets of antimicrobials. We find that the overall survival of mutations that eventually become clinical isolates is strongly determined by the fitness of the bacteria in the presence of the drug (the “resistance level”) and by the fitness of the bacteria without the drug (the “fitness cost”). Using simulation and population genetics theory, we then predict the survival probability of these mutations under different selective regimes defined by drug combination, concentration and dosing, and as well as by the population structure of the bacteria. These predictions are validated by lab evolution and data from clinical isolates. Altogether, by driving the bacterial populations into a region of the landscape where they are unable to grow, we can delay drug resistance.



Almer Van Der Sloot (laboratoire de M Tyers)
Université de Montréal

A synthetic biology platform to generate and screen natural product-like chemical space for novel antibiotic activities

The widespread emergence of antimicrobial-resistant (AMR) pathogens represents one of the most urgent challenges in modern medicine and novel antimicrobials will be required to combat this crisis. Natural products (NPs) encompass an enormous chemical diversity with privileged biological activities and have proven by far the richest source of antibiotics. Over the past three decades, however, emphasis has shifted away from the use of NPs in antibiotic discovery towards synthetic chemical libraries, due in part to isolation, dereplication, resupply and chemical tractability issues associated with NPs. To solve issues traditionally associated with NP-based antibiotic discovery, we have developed a Saccharomyces cerevisiae platform for heterologous production of NP-like chemical matter, termed synthetic natural products (SynNPs). This approach leverages the availability of hundreds of thousands of NP biosynthetic genes (BSGs) in sequence databases and low-cost de novo DNA synthesis, enabling the creation of a large collection of codon- and GC-content optimized NP biosynthetic genes (BSGs) from plant, fungi and bacteria. We designed a programmable yeast artificial chromosome (YAC) assembly method to enable the creation of highly diverse combinatorial libraries that can potentially biosynthesize a massive number of NP-like compounds. These SynNP libraries are then screened in a yeast cell microfactory format using either target-based genetic selection screens or bacterial co-culture assays. Active clones are characterized by a combination of high-throughput metabolomics and activity-guided purification. The SynNP platform will allow the exploration of extensive new-to-nature NP-like chemical space for novel antimicrobial activities in a cost-effective, scalable and sustainable manner.



Gerry Wright
McMaster University

Antibiotic and anticancer resistance from the environment to the human microbiome

Antibiotic and anticancer resistance from the environment to the human microbiome Microbes respond to the presence of toxic compounds using a number of different strategies ranging from active efflux of noxious molecules to their enzymatic transformation to benign metabolites. These mechanisms can have dramatic effects in the case of resistance to antibiotics for example that leads to drug failure. Increasingly we are coming to realize that many anticancer drugs are also susceptible to such activity with impacts on drug efficacy. Components of both human and environmental microbiomes are capable of these transformations, often though different mechanisms. Our efforts to explore this diversity using the examples of the anticancer drug doxorubicin and the antibiotic rifampin will be presented.