Expositor	Work Title	Abstract
Benny Giovanni Cazarín-Santos giovanni.cazarin@gmail.com Escuela Superior de Medicina del Instituto Politécnico Nacional	**Genetic variant of the osteoprotegerin gene (OPG) associated with the asymptomatic stage of coronary artery disease in a Mexican mestizo population**	**Introduction:** Subclinical atherosclerosis (SA) is the presence of coronary calcification in the absence of cardiovascular symptoms, is considerate an asymptomatic stage and usually progresses to coronary artery disease. However, currently the development of strategies for the prevention or identification of this stage is scarce. Studies have reported an association of the osteoprotegerin (*OPG*) gene polymorphisms with vascular calcification process in cardiovascular diseases; nevertheless, to date there are no studies that assess *OPG* polymorphisms in subjects in the asymptomatic stage of atherosclerotic disease. **Objective:** The purpose of this study was to analyze the association of four (rs3134070, rs3134069, rs2073618, and rs3102735) genetic variants and haplotypes of the *OPG* gene with the development of SA and performed an in silico analysis in order to identify the potential functional effects of these genetic variants. **Methodology:** Using Taq-Man genotyping assays, 1413 asymptomatic participants (1041 controls and 372 individuals with SA) were analyzed. In addition, we made an in silico analysis employing bioinformatic analysis to identify response elements for transcription factors in these genetic variants. **Results:** Similar distribution in the frequencies of the *OPG* gene polymorphisms (rs3134070, rs3134069, and rs2073618) were found in subjects with SA and healthy controls. However, the rs3102735 polymorphism showed a lower risk of SA (OR= 0.693, 95% CI= 0.493 – 0.974, *p* heterozygote = 0.035; OR= 0.699, 95% CI=0.496 – 0.985, *p* co-dominant1 = 0.040) and two haplotypes were associated with SA, one as decreased risk: *GACC* (OR= 0.641, 95% CI= 0.414 – 0.990, *p*= 0.045) and the other as increased risk: *GACT* (OR= 1.208, 95% CI = 1.020 – 1.431, *p*= 0.029). Also, the bioinformatic analysis for transcription factors, showed binding sites for the C/EBP-β and C/EBP-α factors in the rs3102735 polymorphism. **Conclusion:** Our results suggest that the rs3102735 polymorphism appeared as a protective marker for SA. This study contributes to the knowledge in the field of molecular cardiology with the clinical interest of developing future panels of genetic markers of atherosclerotic disease, in asymptomatic individuals, for use in preventing its progression.
Dr. Raul Cuauhtemoc Baptista Rojas. raul.baptista@cutonala.udg.mx Centro Universitario de Tonalá, Universidad de Guadalajara, México.	**Type 2 diabetes in Mexican population is associated with HLA-A and HLA-C variants**	Type 2 diabetes has been linked to the expression of human leukocyte antigens, principally to the major histocompatibility complex class II and only scarce reports to major histocompatibility complex class I in specific populations. The objective of the present work was to explore the presence of polymorphisms in the MHC class I related to type 2 diabetes in Mexican population using the GWAS SIGMA database. This database contains information of 3,848 Mexican individuals with type 2 diabetes and 4,366 control individuals from the same population without clinical or hereditary history of the disease. The searching criteria considered a P value < 0.005 and odds ratio > 1. Ten novel statistically significant nucleotide variations were identified: four polymorphisms associated with HLA-A (A * 03: 01: 01: 01), and six with HLA-C (C * 01:

		02: 01: 01). These alleles have a high prevalence in Latin American populations and could potentially be associated with autoimmunity mechanisms that participate in the development of T2D complications. This relationship could explain some phenomena related to the age of initial presentation of the symptoms, its progression and the severity of the damage in target organs.
Jorge Adrian Islas joarian96@gmail.com Instituto Nacional de Medicina Genómica, México.	**Genes associated to maximum lifespan in mammals are more closely associated to genes involved in post mitotic maintenance than to genes involved in cellular**	México Work over the past years has identified distinct genes sets associated with either post mitotic cellular longevity, cellular senescence or maximum lifespan in mammals. However the functional links between these groups of genes so far remains unclear. Using available human gene expression data we use coexpression analysis to assess the possible functional association between these groups of genes. We found that while the collective correlation between genes associated to maximum lifespan in mammals and cellular senescence is no greater than chance expectations in several groups of human tissues, lifespan associated genes display a level of collective correlation with cellular longevity associated genes than expected by chance. These results suggest a closer functional link between genes involved in maximum lifespan and genes involved in post-mitotic cellular longevity in human tissues.
Lourdes Beatriz Cajica Maceda A01732177@tec.mx ITESM, México.	**Sample-specific Transcriptional Network Reconstruction for Breast Cancer**	Abstract – Transcriptional networks are robust tools to study complex phenotypes such as cancer. They provide a unified framework to study biological properties through the analysis of network properties. Classical methods have been able to reconstruct networks from many samples to describe a single phenotype; however, recently developed methods are now focused on the question of reconstructing networks for individual samples. This approach is important, as it may lead to a better understanding of cancer heterogeneity and match transcriptional phenomena to specific clinical features. A current issue with single sample network reconstruction is the fact that the inherent algorithmic complexity of the problem increases in such a way that it makes large-scale genome network reconstructions unfeasible. In this work, we have taken the LIONESS algorithm, which is based on the calculation of pairwise mutual information from gene expression experiments, and adapted it for an HPC setting. Through the use of parallel computing techniques and memory management, we have maximized the computational performance to set the processing time within an 8-hour-window for samples with up to 19556 genes. We provide a case study analyzing a set of 518 breast cancer samples classified by subtype, constructing

		networks of the PAM50 gene signature (50 genes) for each sample. We show that the resulting networks exhibit variability in centrality measures such as degree and betweenness centrality, capturing changes in the importance of network connectivity of individual genes in individual samples of breast cancer.
Armando Ocampo del Valle armando.ocampo@ibt.unam.mx Facultad de Nutrición, Universidad Autónoma del Estado de Morelos, México.	**Evaluation of single nucleotide polymorphisms associated with the development of vascular dementia in the cellular context of the neurovascular unit** *	Vascular dementia is a neurological disease characterized by the declive of at least one cognitive domain of the patient. Its origin is related to a set of cardiovascular pathologies that limit the supply of oxygen and glucose to the central nervous system. Within these nosological entities is atherosclerosis, which is a chronic inflammatory disease of the blood vessels, characterized by the deposition of low-density lipoproteins in the intimal layer of the arteries, generating a lesion called atheroma. It has been proposed that the obstruction of blood flow in the brain is mediated by the formation of thrombi derived from the rupture of the atherosclerotic plaque. The following question was raised in this project. Is it possible to know the relationship of genetic variants associated with atherosclerosis with the development of vascular dementia in the cellular context of the neurovascular unit? To answer this problem, a seek for single nucleotide polymorphisms derived from genome-wide association studies for both diseases was made using the SVA v0.11 algorithm. Subsequently, the type of genetic variant and its topology in the genome was determined. The cell line of the neurovascular unit associated with each polymorphism was identified using SCRAD v0.9, which is a text-mining tool. Likewise, the relationship of these variants with metabolism was evaluated through the information from the REACTOME database. Finally, an *in silico* characterization of the effect of the variants present in genes at the protein level was carried out using POLYPHEN2, PROVEAN, and SIFT. The data presented in this project identify oligodendrocytes and astrocytes as the head cell types in the development of vascular dementia. In the same way, it is detailed that the variants found participate in the metabolic pathways of extracellular matrix degradation, demyelination, and cell death. Highlighting that these events can play an essential role in the etiology of the disease.

Dra. Areceli Vences aritaven@yahoo.com.mx National Institute of Pediatrics, México	**Aberrant expression of cytochrome P450 2W1 in pediatric soft tissue sarcomas: a possible novel therapeutic target**	**Background:** New therapeutic targets for pediatric soft tissue sarcoma (STS) treatment are critically necessary. Human CYP2W1, a recently discovered cytochrome P450 enzyme, has been associated with tumorigenesis and has been proposed as a potential target for anticancer therapy. Here, we investigated aberrant CYP2W1 expression in pediatric STS and its associations with clinicopathological patient data. **Material and methods:** Forty-two primary STS tissues were evaluated for the expression of CYP2W1 mRNA and protein with qRT–PCR and Western blot, respectively. **Results:** CYP2W1 was significantly overexpressed at the mRNA (69%) and protein (38%) levels in STS tissues compared to scarce/absent tissues ($p < 0.05$). CYP2W1 expression in STS was significantly associated with TNM staging ($p < 0.05$). **Conclusion:** CYP2W1 is abnormally expressed in pediatric STS and is associated with tumor progression. Our results could support the use of CYP2W1 as a promising target for novel anticancer therapy.
David Giron Villalobos davidgironvillalobos@gmail.com Instituto Nacional de Medicina Genómica, México.	**Computational modeling of the gut microbiota metabolism in COVID-19 patients**	The current pandemic caused by SARS-COV-2 infection poses a public health problem. Although it was first treated as a respiratory disease, it is now established that it can affect other tissues, for example the gut. This virus can bind the ACE2 receptor and enter the host cells, this receptor is highly expressed in the intestinal tissue specifically in enterocytes. Also, it was found in feces of infected patients. This information raises interest to discover the role of gut microbiota in the development of COVID-19. Nowadays, most of the research is focused on gut microbiota composition and little is known about the interactions in the bacterial community. We used metagenomic shotgun sequencing data from fecal samples of 15 patients, 15 controls and 6 non viral pneumonia taken from Zuo et al, 2020. For the metabolic analysis we used MICOM , a metabolic modeling computational tool, to predict interactions based on metabolic fluxes at a community level. First, we performed multidimensional and differential expression methods for the identification of particular bacteria for each COVID-19 stage. Then, we obtained bacterial interactions, either competition or cooperation, with MICOM, and identified important nodes in the interaction networks. Given this data we compared it with the differential analysis to identify specific bacteria for each COVID-19 stage. For example, akkermansia is found as a competition hub in critical patients as well as lactobacillus and parabacteroides. Further, we obtained the net metabolic fluxes for short chain fatty acids and we observed that butyrate was decreased for the COVID-19 patients in comparison with

		the healthy group. This study allows us to better understand how interactions at community level can participate in the development of this disease and its different clinical stages, from a metabolic perspective.
Bertha Rueda-Zarazúa bgrueda@inmegen.edu.mx INMEGEN, UNAM, México	**Exploring somatic mutations in mexican patients with lung adenocarcinoma**	In 2020, lung cancer was the first cause of mortality worldwide and 4th in Mexico. Despite all efforts, this disease still has one of the highest mortality rates. Lung cancer is broadly classified into small cell lung cancer (SCLC, 15%) and non-small cell lung cancer (NSCLC, 85%) from which lung adenocarcinoma is the most common subtype in Mexico and around the world. Somatic variants in driver genes and their frequencies have been reported to vary among different populations, these disparities may be related to differences in risk factors and genetic background. Mexico is a country with ethnic diversity and lower smoking incidence than other countries. Other specific risk factors have been described, such as wood-smoke exposure. The objective of this work is to identify somatic mutations related to lung adenocarcinoma in mexican patients and their association with clinical variants. Using samples from mexican patients with lung adenocarcinoma (FFPE and frozen tissue) we are doing WES for the identification of variants to describe the similarities and differences between this population to others and to identify the correlation with clinical variables as age, gender and risk factors. This is a work in progress. As part of our preliminar results, some of the mutations present in the analyzed samples are mutations identified previously in other populations as rs121913529 in KRAS and rs121913229 in exon 19 of EGFR. Other samples appear to lack mutations in common driver genes. Knowledge about frequencies and genes affected by driver mutations provides relevant information about available target therapies, as part of precision medicine.
Cristian Mendoza-Ortiz cristian.mendoza1996.cmo@gmail.com INMEGEN, México	**Computational modeling of the dynamics of the gut microbiota metabolism**	The dynamics of the gut microbiota are primarily affected by abrupt changes in diet, infection events, and antibiotic therapy. Understanding the mechanisms behind these transitions is critical to generating predictions regarding personalized interventions in these microbial communities. Mathematical modeling allows a holistic study of complex systems like this one, based on data from genomic technologies. Recently, ecological models, such as the compositional Lotka-Volterra (CLV), have been used to represent the growth and interactions between taxa in these systems (Joseph et al., 2020). However, when the metabolism drives compositional changes, these models are limited. In this work, we analyzed the dynamics of the metabolism of the gut microbiota in a longitudinal database through a hybrid model between CLV and flux balance analysis (FBA). To do this, we compared the performance of 4 dynamic models

		through 'leave-one-out' cross-validation using the RMSE as a proxy of the prediction error. From these evaluations, CLV was chosen for its low RMSE and for the possibility it offers to carry out analyzes directly from relative microbial abundances. Then, we tested two approaches between CLV and MICOM. The latter is an FBA-type computational tool that includes maximization processes and the definition of a balance between community growth and individualized growth of each microorganism (Diener et al., 2020). Finally, from this model, we will characterize metabolites produced differentially by these communities and the stability of the enterotypes. Furthermore, we will simulate the metabolic response of the system under different disturbances.
Eliezer Flores-Garza eliezerafg@gmail.com IIB-UNAM	**Mathematical model of the immunopathological progression of tuberculosis**	Tuberculosis (TB) is a worldwide persistent infectious disease caused by bacteria from the Mycobacterium tuberculosis complex. It is one of the top 10 causes of death worldwide and approximately a quarter of the world's population is latently infected. Efficient treatments are difficult to establish as there is insufficient understanding of the molecular mechanisms behind the immunopathological progression of the disease. Using an integrative systems biology approach, we study the immunopathological progression of TB, analysing the key interactions between the cells involved in the infectious process. We integrated multiple in vivo and in vitro datasets from immunohistochemical, serological, molecular biology and cell count assays into a mechanistic mathematical model. Our ODE model captures the regulatory interplay between the phenotypic variation of the key cellular players involved in the disease progression and the inflammatory microenvironment. The model reproduces in vivo time course data of an experimental model of progressive pulmonary TB in mouse, accurately reflecting the functional adaptations of the host-pathogen interactions as the disease progresses through three phases: 1: innate immune response, 2: adaptive immune response and 3: anti-inflammatory response. We used the model to assess the effect of genotypic variations encoded as changes in parameters on disease outcomes and consistently found an all-or-nothing response, where the virtual mouse either completely clears the infection or suffers an uncontrolled Tb growth. Results show that it is 84% probable that mouse submitted to a progressive pulmonary TB assay will end up with an uncontrolled infection. The simulations also show how the genotypic variations shape the transitions across phases. All genotypes evaluated eventually progressed to phase 2 of the disease, suggesting that adaptive immune response activation is unavoidable. When stationed in phase 2, the infection was cleared. The anti-inflammatory conditions that characterize phase 3 have the

		highest probability of leading to uncontrolled bacterial growth; in contrast, the pro-inflammatory genotype associated with phase 2 has the highest probability of bacterial clearance. 42% of the genotypes evaluated showed a bistable response, with one stable steady state corresponding to infection clearance and the other one to uncontrolled bacterial growth. Together, our analysis suggests that initial conditions in bacterial and macrophage loads coupled with the inflammatory microenvironment play a key role in determining the outcome of the disease. It is step forward in understanding the mechanisms that shape TB progression.
Sophia Orozco fs.orozcoruiz@gmail.com International Laboratory for Human Genome Research (LIIGH) UNAM	**Expression and Evolutionary Dynamics of a Genetic Circuit with Positive and Negative Feedback Loops**	What evolutionary conditions select for specific genetic circuit dynamics remains an open question. Here, we characterize the expression dynamics of a genetic circuit capable of oscillations and bistable epigenetic switching in the presence of noise, with particular interest in noise-induced emergent properties. Then, using an evolutionary model we explore the potential of those dynamics as strategies to deal with fluctuating environments while in competition between them and genetic adaptation.
Cristian Padron-Manrique cristianjuliocesar.agualimpia@gmail.com INMEGEN, México	**Diffusion on PCA-UMAP manifold captures a well-balance of local, global, and continuum structure to denoise single-cell RNA sequencing data**	Single-cell transcriptomics (scRNA-seq) is becoming a technology that is transforming biological discovery in many fields of medicine. Despite its impact in many areas, scRNASeq is technologically and experimentally limited by the inefficient transcript capture and the high rise of noise sources. For that reason, imputation methods were designed to denoise and recover missing values. Many imputation methods (e.g., neighbor averaging or graph diffusion) rely on k nearest neighbor graph construction derived from a mathematical space as a low-dimensional manifold. Nevertheless, the construction of mathematical spaces could be misleading the representation of densities of the distinct cell phenotypes due to the negative effects of the curse of dimensionality. In this work, we demonstrated that the imputation of data through diffusion approach on PCA space favor over-smoothing when increases the dimension of PCA and the diffusion parameters, such *k-NN* (*k-nearest neighbors*) and *t* (value of the exponentiation of the Markov matrix) parameters. In this case, the diffusion on PCA space distorts the cell neighborhood captured in the Markovian matrix creating an artifact by

		connecting densities of distinct cell phenotypes, even though these are not related phenotypically. In this situation, over-smoothing of data is due to the fact of shared information among spurious cell neighbors. Therefore, it can not account for more information on the variability (from principal components) or nearest neighbors for a well construction of a cell-neighborhood. To solve above mentioned issues, we propose a new approach called sc-PHENIX(***s**ingle **c**ell-**PHE**notype recovery by **N**on-linear **I**mputation of gene e**X**pression*) which uses PCA-UMAP initialization for revealing new insights into the recovered gene expression that are masked by diffusion on PCA space.
Dra. Elisa Domíguez-Hüttinger Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México	**Mathematical modelling of the regulatory mechanisms of keratinocyte differentiation for epidermal homeostasis**	The epidermis is formed by layers of keratinocytes with increasing levels of differentiation towards the outer skin. Regulation of keratinocyte differentiation across the epidermis is crucial for the homeostasis of the skin barrier that protects our body from environmental stressors and dehydration. Keratinocytes need to be terminally differentiated when they reach the outer layer to express components that constitute the skin barrier. Timely keratinocyte differentiation across all epidermal layers requires robust regulatory mechanisms. Keratinocyte differentiation is triggered by skin barrier damage via changes in extracellular calcium at a lower epidermal layer. Inflammation and immune responses can modulate this differentiation process by interfering with the calcium-activated signalling networks. Understanding how these micro-environmental conditions shape keratinocyte differentiation is necessary to unravel how epidermal homeostasis is maintained. However, such regulatory mechanisms are still not clearly understood due to difficulties in performing quantitative experiments at the individual cell level in a stratified multi-layered tissue. Here we investigate the key regulatory mechanisms of keratinocyte differentiation through mathematical modelling. We developed a minimal mechanistic model of keratinocyte differentiation by integrating experimental results from manually curated 96 publications and then applying model reduction and global parameter optimization. The key regulatory structure of the model is characterized by positive feedback with cooperativity between Np63 and Stat3, two master regulators of keratinocyte differentiation. This control structure gives rise to a history-dependent and switch-like dose-response behaviour between extracellular calcium and the expression of terminal differentiation markers which is consistent with the in vitro differentiation of keratinocytes observed in calcium switch experiments. Our model analysis demonstrated that immune responses and inflammation perturb

		keratinocyte differentiation by shifting the thresholds for differentiation and de-differentiation towards lower calcium concentrations, suggesting that environmental aggressors increase the sensitivity of the keratinocytes to skin barrier perturbations. How skin microenvironments trigger the dynamic regulation of keratinocyte differentiation will help understand the consequences of skin diseases such as atopic dermatitis and psoriasis on skin barrier homeostasis.