Project 1: Curta-metragem: "Vozes da Névoa"

O projeto “Vozes da Névoa” pretende fazer uma exploração da pesca do bacalhau nos bancos da Terra Nova pelos portugueses, assim como a sua relação com a emigração lusitana para os EUA em meados do século XX. Para isso, realizer-se-ão entrevistas com antigos bacalhoeiros portugueses residentes em New Bedford, com o objectivo de completar uma curta-metragem documental.

Project 2: Metabolic Reprogramming in the Offspring of Insulin Resistance Parents

Project Goals: the main goals of this internship at the Joslin Diabetes Center (JDC) are 1) to understand the impact of *in utero* insulin resistance on physiology in the adult offspring 2) to understand paternal-induced metabolic changes in the offspring of insulin resistant fathers.

Summary of background and importance of diabetes studies: Diabetes mellitus is a metabolic disease that is mainly characterized by an abnormal raise in plasma glucose concentration. The etiology of the disease is vast and the complications lead to morbidity. Type-1 diabetes (T1D), or insulin- dependent diabetes, is acute, progresses quickly and is characterized by a complete insulin deficiency due to the loss of pancreatic beta cells by various factors (e.g., virus, environmental). Type-2 diabetes (T2D), or non-insulin-dependent diabetes, which was reported to be restricted to adults and elderly individuals, is now also recognized in adolescents due to undetermined factors [1]. Diabetes mellitus is increasing worldwide and by 2030 is expected to affect 366 million people [2]. During 2012 the total estimated cost of diabetes care in USA was 220 billion euros and represented more than 20% of the total health care budget [3]. On the other hand, 12.4% of the Portuguese population lived with diabetes in 2009. This resulted in an estimated total annual cost of 1.3 billion euros, representing 11% of the Portuguese healthcare budget [4]. Despite the identification of more than 100 genes conferring risk of diabetes, only a small portion of the disease risk can be ascribed to the genes. As progression to T2D is largely due to insulin secretory dysfunction and significant beta-cell loss, further research in understanding the epigenetic modifications in offspring beta-cells of insulin resistant parents, will likely play an important role in determining how elevated levels of insulin and glucose itself, influences the expression of important genes in beta cell function and survival.

Project 3: CRISPR/Cas9-based therapeutics for Friedreich's ataxia

O laboratório está inserido no Center for Human Genetic Research (Massachusetts General Hospital / Harvard Medical School) e tem como interesses de investigação os mecanismos genéticos e moleculares causadores de doenças neurodegenerativas como a Ataxia de Friedreich Ataxia (FA) e a doença de Huntington (HD).

FA é uma doença genética rara causada por uma repetição de trinucleótideos GAA que quando expandida resulta num silenciamento genético e consequente redução nos níveis de frataxin.

Em particular, o projeto deste estágio envolve o uso de modelos celulares e técnicas de engenharia genómica com o objetivo de aliviar o silenciamento genético na origem de FA.

O Estagiário vai ser treinado numa série de técnicas laboratoriais de forma a conduzir experiências preliminares que visam desenvolver e validar reagentes capazes de ativar de forma específica a expressão do gene frataxin. Tais técnicas incluem elementos básicos de biologia molecular (extração de DNA, PCR, quantificação de expressão genética, gel eletroforese), cultura de células humanas, transfeções, e CRISPR Cas9.

Project 4: Testing clinically relevant matrices for Schwann cell transplantation following spinal cord injury

Cell therapy strategies to repair the injured spinal cord are promising new breakthroughs with the recent clinical trials in acute and chronic spinal cord injury (SCI) subjects [1]. Following an insult to the mammalian spinal cord, a series of complex responses follow that contribute to an aggravated expansion of the initial injury, and result in dramatic functional deficits [2]. The formation of fluid-filled cavities contributes, in part, to the regenerative failure and functional deficits that follow SCI. Cell transplantation strategies rely on reducing cavitation following damage, re-bridging the injured tissue and creating more favorable conditions for axonal regeneration. From the various cell types proposed to be used in SCI repair, Schwann cells (SCs) have been extensively studied and are currently undergoing safety and efficacy evaluation in clinical trials in the Miami Project to Cure Paralysis. SCs are the myelinating glia of the peripheral nervous system, and can be obtained from SCI patients, expanded in culture, and autologously transplanted into the lesioned spinal cord. These cells were found to be neuroprotective, reduce cavitation, promote axon regeneration and myelination, and modestly improve hindlimb movements in animal models [3, 4]. Nevertheless, one of the hurdles that may be limiting the therapeutic potential of SC implants, as well as other cell types, is the poor survival rate of the transplanted cells in the injury site [5]. Previous reports have shown that after a contusion injury in rats, there is about an 80% SC loss 3 weeks after transplantation due to necrosis and apoptosis [6, 7]. The traumatic nature of cell isolation procedures, the detachment from its extracellular matrix (ECM) before transplantation, and the injury environments are some factors that contribute to this significant cell death.

One possible approach to improve transplanted SC survival, therefore maximizing its therapeutic potential, is to implant them in ECM-derived substrates, such as an injectable matrix, instead of the culture media suspension approach. Most commercial ECM matrices, however, are tumor-derived and have undefined and variable growth-factor composition. For these reasons, they are not clinically applicable and it still remains of the utmost importance to identify clinically relevant injectable matrices for achieving greater survival and efficacy of cellular implants after SCI. **The goal of this project** is to evaluate the potential of ECM-derived matrices in supporting SC survival after injury, while fostering neuronal regeneration through the graft. It will be a project involving concepts and techniques from biomaterials and biomedical research, and envisioning future translational studies for clinical applications.

Project 5

Measurements of chemical abundances in local galaxies are different from measurements along single sight lines because light from all the stars in the galaxy is collected as if the galaxy was a single point source. These stars probe different portions of a galaxy, some with different chemical abundances and physical conditions, and can hide saturation effects. Spectra of local galaxies might also have low S/N, which further compounds the problem. This project consists of assessing the saturation effects in abundance measurements of extragalactic sight lines by using nearby stars to measure abundances in each sightline individually as well as in the combined spectrum of all the stars, to simulate a galaxy spectrum. The measurements will use the apparent optical depth technique on echelle data obtained with the Space Telescope Imaging Spectrograph (STIS) onboard the Hubble Space Telescope (HST).