

The partners of the INTERREG project TRAIN (Big Data and Models of Diseases), kindly invite you to the lectures of Luca Braga and Serena Zacchigna from the *International Centre for Genetic Engineering and Biotechnology (ICGEB)*, Trieste that will take place at **Jozef Stefan International Postgraduate School** in Ljubljana (Jamova cesta 39) on **Friday, 25 MAY 2018, 10:00-11:30**. The abstracts of the talks are as follows.

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### **High Content Screenings: From Large Libraries to Functional Hits**

**Luca Braga**, *International Centre for Genetic Engineering and Biotechnology (ICGEB)*, Trieste, Italy

Image-based high content screening is a powerful tool to gain systematic measurement of cell phenotype perturbation upon a given treatment. The combination of this technology with RNA interference, CRISPR-Cas9 and small molecules generates a comprehensive method to decipher and eventually tune complex biological processes, such as changes in cell morphology, cell and proliferation. This has been made possible by the availability of innovative robotics, imaging and computational systems, increasing the scale and the speed of the analysis.

High content fluorescent microscopes allow to systematically assess the expression and the localization of multiple biomarkers, which can be imaged simultaneously using different wavelengths. The integration of high content imaging with automated image-analysis allows tracking multiple physical and logical parameters, thus generating a multi-dimensional picture of any biological process. I will describe several examples of image-based high content screenings, which allowed us to successfully identify functional hits starting from large collections of molecules of unknown function.

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### **Novel genes for old hearts**

**Serena Zacchigna**, *International Centre for Genetic Engineering and Biotechnology (ICGEB)*, Trieste, Italy

The burden of cardiovascular disease is enormous, largely as a consequence of the aging of the population, the incapacity of the heart to regenerate once damaged and the lack of novel drugs over the last 20 years. Thus, there is an impelling need to develop novel therapeutic strategies aimed at inducing cardiac repair and regeneration. In contrast to other species that regenerate the heart during the adult life, in mammals, damage to the myocardium is mended by a scarring mechanism. However, multiple evidence now indicates that a limited capacity of myocardial renewal also exists in adult individuals, and we are therefore actively searching for factors able to foster this regenerative capacity. Using viral vectors based on the Adeno-Associated Virus (AAV), which transduce the heart at very high efficiency, we are undertaking an exhaustive approach to identify extracellular proteins promoting cardiac repair, selected from an AAV library corresponding to the mouse secretome (1200+ secreted proteins). A second approach entails high throughput screening of microRNAs promoting cardiomyocyte proliferation. Starting from a whole genome human microRNA library, we have identified a few microRNAs endowed with the capacity of promoting expansion of cardiomyocytes in cell culture, inducing massive cardiac hyperplasty in the neonatal heart and improving cardiac function after myocardial infarction. These microRNAs function by directly activating the proliferative potential of differentiated cardiomyocytes, thus bypassing the requirement of stem cell expansion and differentiation.

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