All multicellular organisms derive from the single cell – the zygote – formed through a fertilization. During the embryonic development, from this cellular unit endowed with an astonishing plasticity, all the tissues of the adult body will be formed. This remarkable feat is tightly controlled, with subsequent molecular cascades being temporally switched on and off with a surgical precision.

Initially fully plastic (totipotent) cells specialize into those giving rise to the extraembryonic tissues, including placenta, and embryonic stem cells from which the whole body will be derived. Development of the embryonic stem cells is well kept in check – despite presence of the developmental malformations, in a vast majority of cases a healthy, fully-formed being is born, with functional tissues as different as bones, blood, muscles or brain. Mechanisms that govern embryonic development are subject to the interest of humanity already since times of Hippocrates and Aristotle, with his *De generatione animalium* (*On the Generation of Animals).* In recent years thanks to the unprecedented methodological advancements, we constantly obtain new insights into discrete steps of the embryonic development, and many mechanisms that govern them. These are extremely valuable given the translational aspect of such research for the regenerative and reproductive medicine. Despite all the ongoing research, we still lack the wholesome outlook into many of the mechanisms that keep embryonic development in check.

Our new observations indicate that one of the processes required for a proper function of embryonic stem cells is splicing. Splicing is a molecular process that acts as an amplifier to boost amount of information encoded by the single gene. During splicing parts of the ribonucleic acid (RNA) are cut and stitched to produce new variants and types. That enables creation of multiple proteins on the matrix of the single gene. Molecular scissors that are responsible for splicing consist of complex macromolecular machinery, termed spliceosome. Spliceosome is the largest conglomerate in the cell, composed of hundreds of proteins. In this project, we propose that differential expression levels of individual spliceosomal proteins may affect spliceosome function. We further posit that this regulation may be critically important for the biology of embryonic stem cells that rely on the quick re-wiring of the specific cellular cascades to meet demands of the healthy differentiation.

In the proposed project we will analyse expression profiles of spliceosome proteins during early activation and differentiation of embryonic stem cells. We will delineate how these regulated levels may impact splicing to determine developmental routes. In the last stage, we will determine how regulation of the splicing instructs the fate of embryonic stem cells and their differentiation trajectories. To delineate all these dependencies, we will employ an ensemble of proteomic approaches, *in vitro* and *in vivo* experiments coupled with genome editing technologies.

Through the proposed research program, we want to understand how individual components of the spliceosome are regulated during critical stages of the embryonic development. We hope to not only determine the molecular underpinnings of organism formation, but also to shed new light on how they may interface with diseases originating during this highly sensitive stage of the life.