Dana-Farber Cancer Institute | Boston Children's
Dana-Farber/Boston Children's Cancer and Blood Disorders Center

HARVARD MEDICAL SCHOOL
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Research Interest:

Throughout my training as medical biotechnologist, I have focused since my early career in the field of gene therapy and gained extensive experience on the development of innovative gene transfer technologies based on engineered nucleases. Working with the group of Luigi Naldini at the San Raffaele Telethon Institute for Gene Therapy, I contributed to pioneer this field since when ZFNs were first shown to enhance gene targeting and be useful for genetic engineering of somatic cells for therapeutic purposes. In 2007, I contributed to a break-through work where we demonstrated for the first time the possibility to exploit ZFN to direct the integration of exogenous DNA sequences into a predetermined genomic locus of several human cell types (Lombardo, Genovese et al., Nat Biotech 2008). During my Ph.D. studies, I extended my knowledge and skills on this technology by developing the T cell receptor gene editing strategy to improve safety and efficacy of cancer adoptive immunotherapies (Provasi* Genovese et al., Nat Med. 2012). This innovative approach is now widely used in the immunotherapy field for generating allo-compatible T cells or to express CAR genes under the control of endogenous TCR promoter. As post-doctoral associate, I engaged an ambitious study aimed to correct inherited mutations and developed the first protocol that allow targeted transgene integration in human hematopoietic stem cells (HSC) capable of long-term multilineage repopulation (Genovese at al., Nature 2014). By assuming a more senior role on the project, I coordinated a work team of scientists towards the goal to perform pre-clinical development and proof of feasibility of these novel medical treatments for some candidate diseases, chosen as paradigmatic for testing their therapeutic potential. I coordinated the scientific activity of the projects and actively contribute to secure financial support and managing collaboration with both academic and industrial partners. My first project conducted as principal investigator focused on the HDR-mediated correction of HIGM1 is now in advanced phases of manufacturing development, and we expect to open a first-of-this-kind trial in two years from now. Recently, I have established my own independent laboratory at the Dana-Farber/Boston Children's Cancer and Blood Disorder Center, and been appointed assistant professor at Harvard Medical School. As an early stage investigator, I am keenly interested in overcoming obstacles currently hampering full exploitation of HDR-driven editing in human lymphocytes and HSPC, and apply these innovative tools for developing new therapeutics. This extended scope matches well my prior scientific training in cancer immunotherapy and T cell and HSC engineering. My impression is that now that the HSC gene editing technology is approaching clinical testing for relatively straightforward problems like monogenic blood diseases, scientists have to higher the bar to reach new solution for more complex disorders, such as onco-hematologic disorders.

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