SickKids | PETER GILGAN CENTRE FOR RESEARCH AND LEARNING

Models of Congenital Malformation and Disease

Faculty Search Seminar

Dr. Bin Gu

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2-cell based genome editing – from embryonic development to disease modeling

CRISPR has changed mouse genetics by enabling rapid genetic modifications directly through mouse embryos. Simple modifications such as knockout, point mutation, and small tag insertion can be efficiently achieved by manipulating mouse zygotes, more complex alleles such as reporters, conditional alleles, humanized alleles, and chromosome abnormalities are still challenging. Taking advantage of the unique cell cycle profile and DNA repair mechanisms at the 2-cell stage of mouse embryos, I have developed a series of genome editing technologies, including two cell (2C)-Homologous Recombination(HR)-CRISPR and two cell(2C)-Proximal Recombination(PR)-CRISPR. These technologies have enabled the generation of complex genetic modifications in mice efficiently, and opened up broad new opportunities in biomedical research, particularly in two areas, 1) using quantitative live imaging to interrogate the regulatory mechanism of normal development and congenital malformations in real-time, and 2) studying mechanisms and developing therapeutic strategies for congenital diseases using mouse models faithfully recapitulate human mutations. I will first present the development of 2C-HR-CRISPR technology, and the discoveries and insights on the regulatory mechanisms of normal embryonic development gained by live imaging reporter embryos. A particular focus will be placed on Yap mediated signaling in embryonic development. Then I will present our recent efforts in modeling complex mutation mediated human disease. A particular focus will be placed on the development of 2C-PR-CRISPR technology and the generation and characterization of genomic duplication disease models, including the first *MECP2* duplication mouse model. In the third part of the talk, I will discuss the future directions of my research program on modeling and therapy development of congenital diseases, including some preliminary study on the dynamic mechanosensitive Yap signal regulation of fetal bone development by live imaging, and their potential implication in skeletal dysplasia.

Monday | February 3rd | 2020 | 3 pm

PGCRL Event Room 1

Hosts: Drs. Brian Ciruna & John Brumell

Dr. Bin Gu is being interviewed for a Scientist position at the Research Institute