GENETICS, BIOINFORMATICS, AND SYSTEMS BIOLOGY COLLOQUIUM PRESENTS:

THURSDAY NOVEMBER 17
12:00 PM PST

@ LEICHTAG AUDITORIUM RM 107

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PANCREATIC BETA CELL NETWORKS IN HEALTH AND DIABETES

BIOLOGICAL TISSUES ARE COMPRISED OF DIFFERENT CELL TYPES, AND TECHNOLOGIES SUCH AS SINGLE-CELL RNA SEQUENCING AND PATCH-SEQ, CALCIUM IMAGING (FIG.1 A-B) HAVE ENABLED US TO VIEW THE HETEROGENEITY AND DYNAMIC STATES THAT CELLS CAN EXIST IN. FURTHER, SOME CELL POPULATIONS MAY DISPROPORTIONATELY CONTROL OTHER CELLS WITHIN A TISSUE (E.G., 1% OF CARDIOMYOCYTES SPONTANEOUSLY GENERATE ELECTRICAL IMPULSES THAT SET THE PACE OF HEART CONTRACTIONS). RECENTLY SOME INSULIN-PRODUCING "HUB" BETA-CELLS (FIG.1 C) WERE REPORTED TO DISPROPORTIONATELY CONTROL THE FUNCTION OF THE PANCREATIC ISLETS OF LANGERHANS. ISLETS ARE COMPLEX MULTI-CELLULAR STRUCTURES CONSISTING OF INSULIN-SECRETING BETA-CELLS, GLUCAGON-SECRETING ALPHA-CELLS, AND SOMATOSTATIN-SECRETING DELTA-CELLS. THESE CELLS ARE ELECTRICALLY EXCITABLE AND CONTROL GLUCOSE HOMEOSTASIS. DIABETES IS CAUSED BY DYSFUNCTION IN ISLET HORMONE SECRETION. WHEN A "HUB" BETA-CELL IS DISABLED, THE REST OF THE ISLET LOSES THE ELECTRICAL COORDINATION NECESSARY FOR EFFICIENT INSULIN SECRETION. DISCOORDINATION, SIMILAR TO THAT OBSERVED FOLLOWING SILENCING OF THE "HUB" BETA-CELL, HAS BEEN OBSERVED IN ISLETS FROM MOUSE MODELS AND HUMAN DONORS WITH DIABETES. THEREFORE, UNDERSTANDING THE FUNCTIONAL HETEROGENEITY OF BETA-CELLS IS VERY IMPORTANT FOR THE PREVENTION AND DEVELOPMENT OF THERAPIES FOR DIABETES. IN BIOLOGICAL SYSTEMS, COMPLEX BEHAVIOR CAN BE DESCRIBED BY NETWORKS, INCLUDING BRAIN NEURAL NETWORKS, OR THE NETWORKS OF INTERACTING PROTEINS. RECENTLY IT HAS BEEN SHOWN THAT NETWORK PROPERTIES EMERGE IN THE ISLETS OF LANGERHANS. NETWORK THEORY, COMBINED WITH QUANTITATIVE IMAGING TECHNIQUES OFFERS A POWERFUL APPROACH TO INTERROGATING CONNECTIONS BETWEEN THE STRUCTURE AND FUNCTION OF COMPLEX SYSTEMS. I APPLY NETWORK THEORY ANALYSIS, COMPUTATIONAL MODELING, MULTI-SCALE QUANTITATIVE MICROSCOPY, AND SINGLE-CELL TARGETED LASER INTERVENTION TO UNDERSTAND AND PROGNOSIS STRUCTURAL-FUNCTIONAL CONNECTIVITY IN PANCREATIC ISLETS AND DISEASE PATHOGENESIS.

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