Aneuploidy is a state characterized by an abnormal number of chromosomes, which can cause miscarriages and severe developmental disorders. Down syndrome, or Trisomy 21, is a condition caused by an additional copy of chromosome 21. Trisomy 21 leads to intellectual disability, heart defects and Alzheimer's disease, amongst others. Chromosome 21 encodes approximately 230 genes, but surprisingly, cells that contain an extra copy of this chromosome, produce more RNA not only from these genes, but also from genes encoded on other chromosomes. So far, the mechanism leading to these global changes in gene expression is unknown. In this project, I will use stem cells derived from Down Syndrome patients to 1) investigate mechanisms that enable increased production of RNA in Trisomy 21 cells, 2) understand how these cells cope with increased concentration of RNA, and 3) identify the protein factors involved in increased RNA production.
This study will provide insights into the mechanism leading to global gene expression changes in T21 cells and contribute to understanding the involvement of aneuploidy in other diseases, such as cancer. In the longer term, the results of this project may contribute to the development of effective therapies for conditions with abnormal karyotypes.