Schweizerische Anorexia Nervosa Stiftung
Fondation Suisse d'Anorexie Nerveuse
Fondazione Svizzera d'Anoressia Nervosa

Epigenetic Biomarkers of Anorexia Nervosa and Remission
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Authors
Dr. Nicolas RAMOZ, Prof. Sébastien GUILLAUME

Abstract

The main goal of this project founded by the Fondation Suisse d'Anorexie Nerveuse was to identify the expression profiles of the microRNAs (miRNAs) in actual anorexia nervosa (AN) patients and in subjects that evolved to remission (at least one year of BMI>18, called AN remitters). We first screened microRNAs with the Affymetrix miRNA4.0 chip between 24 AN patients and 24 controls. We found several microRAN differentially expressed in AN patients compared to controls. We classified microRNAs increase or decrease in AN patients compared to controls. We also screen the expression of the genes in the same subjects with the GeneChip™ Human Gene 2.0. We observed only a reduced number in expressed genes in the samples. Furthermore, only few genes were reported as expressed in the brain. To confirm and to validate the observations, we also performed a microRNA sequencing and a RNAseq to cover all the expressed genes in a second set of AN patients. These high throughput technics should confirm our previous associated microRNAs and detect also novel microRNAs and also confirm our previous expressed genes associated with AN and detect mutations in the expressed genes. This high throughput strategy is to confirm with different technics the previous results and to cover the whole genome expression. Due to the COVID pandemic, we have delay. We are still analyzing the data. Then, we will repeat these sequencing strategies in a set of AN patients (time zero) that evolved to remission (time 1 year after). Finally, all these results will be completed with the detection of the target protein of at least one gene expressed. To conclude, we will characterize a biomarker, at the epigenetic level with microRNAs, at the molecular level with the gene expression, and at the protein level with the dosage of all of them in the blood of AN patients. This will be helpful for to define the severity of anorexia nervosa and also to have good cue to detect if the AN patient will evolve to the remission and, to adapt the care and treatment in this goal.

Introduction

The main goal of this project was to identify the expression profiles of the microRNAs (miRNAs) in actual anorexia nervosa (AN) patients and in subjects that evolved to remission (at least one year of BMI>18, called AN remitters). The miRNAs impact the expression and the translation of the genes to proteins at the epigenetic level.

Our aims are to characterize specific profiles of miRNA levels in AN for the diagnostic and in remitters for the prognostic. The 10 most differentially expressed miRNAs (increased or decreased between AN patients and remitters) will be used to be validate as prognostic epigenetic biomarkers in a longitudinal cohort where patients are in remission at 1 year and other patients are still current AN.

To date, this is the first study that screen the genome-wide micro RNAs in AN. Furthermore, we also investigate the transcriptomic of the subjects. To date, only few publications report the measure of expression of candidate genes and only one report a whole-genome transcriptomic study in an in vitro human iPSC-derived neurons of AN cases (Negraes et al. 2017) and other publications are only based on correlation with database of gene expression in the general population in link with genetic variants associated with AN (All, Cell 2019; Bryois et al. Nature Genetics 2020).

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