Functional characterization of a mutated gene in a patient with intellectual disability

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Intellectual disability (ID) is a common condition that affects 1-3% of human population. Patients with ID have certain limitations in mental functions, and in skills such as taking care of themselves and communicating with other people. ID can be caused by infections and injuries, but is mostly caused by problems in our genetic material.

Genetic information is stored as sequences in our genetic material, and when a permanent change in these sequences happens, we called it a mutation. Mutations can be inherited from parents, however, ID patients often have genetic mutations that are present for the first time in the family history, which can be caused buy mutations in germ cells (egg or sperm), or in the fertilized egg itself. These kind of genetic changes are called de novo mutations.

In this study, we aim to identify de novo mutations in patients with ID and study how those mutations can affect the normal development of the patients. Our studies may help in treatment of ID, anticipating the development of condition, and enable family plans. Our studies can also generate valuable knowledge on the functions of our genetic materials and the normal development of the human brain.

We identify de novo mutations by sequencing important parts of the genetic material of ID patients and the parents. The genetic material were extracted from the ID patient and the parents, which were sequenced and analyzed to identify the potential disease causing mutations. The patient's sequences were compared to the human reference sequence and the parents' sequences to identify mutations. After filtering out the mutations that were not causative de novo point mutations, we obtained a list of candidate de novo point mutations, which were then validated by other methods.

Recently, we successfully identified and validated a de novo point mutation in a patient with ID. This mutation changes the genetic information on a protein, which, among other things, regulates certain vitamin D related body functions.

Our genetic material contains information on the structures of all the proteins, and when this kind of information is processed in the body to make proteins, we call it the expression of proteins. In this study, blood samples from the patient and the parents were prepared in the clinic, and we tested the expression levels of many proteins, including four vitamin D related proteins. Three of the four vitamin D related proteins were shown to be overly expressed in the patient compared to the parents, which means the patient could have too much of those proteins in the body. One of the overly expressed proteins would lead to abnormally low vitamin D levels. We immediately test the patient's vitamin D level, and the patient is shown to have vitamin D insufficiency.

We have further performed cell culture experiments to confirm that the de novo mutation led to higher expression of vitamin D related proteins, and we are currently performing more experiments to further investigate the de novo mutation.

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