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PRESS RELEASE

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VariantMaster: A software to identify genetic mutations

Under the direction of Professor Stylianos Antonarakis, a research team from the Department of Genetic Medicine and Development of the Faculty of Medicine of the University of Geneva (UNIGE) developed a computer programme to identify mutations causing certain genetic diseases by analysing the genome sequencing data. According to Federico A. Santoni, the principal designer of VariantMaster, this same software can also detect the mutations leading to the appearance of tumours in patients with cancer. These detections are the subject of a publication in the *Genome Research Magazine* and the software itself is available to researchers all over the world.

Under the direction of Professor Stylianos Antonarakis, a research team from the Department of Genetic Medicine and Development of the Faculty of Medicine of the University of Geneva (UNIGE) developed VariantMaster, a computer program to identify mutations causing certain genetic di-seases after analysis of genome sequencing data. According to Federico A. Santoni, the principal designer, this software can also detect the mutations leading to the development of tumors in patients with cancer. VariantMaster is the subject of a publication in Genome Research and it is available to researchers all over the world.

For experts in clinical genetics, the identification of gene¬tic mutations causing certain monogenic disorders can be like looking for a needle in a haystack. A group of resear¬chers from the Faculty of Medicine of UNIGE developed an innovative software for rapidly detecting such deleterious mutations, thereby facilitating molecular diagnosis, and improving medical management for patients affected with genetic disorders, and their relatives.

An immediate success

VariantMaster, freely downloadable from http://sourceforge.net/pro¬jects/variantmaster/, is a tool for the analysis of genome sequencing data for the accurate and efficient identification of causative variants of genetic di¬seases. Close to 100 downloads in a month from China, Israel or the United States demonstrate the interest of the scientific and medical community for this tool which opens up exciting prospects for research and personalized/genomic medicine. VariantMaster was also picked up in the “Research Hi¬ghlight” section of the magazine Nature Review Genetics. If other software analyzing genome sequencing data already exist, it is, as Federico A. Santoni emphasizes, the novel probabilistic approach that makes VariantMaster a really innovative tool. For this probabilistic method, in addition to being very accurate and single-stepped, is able to prioritize the most likely genetic variants involved in a disease among tens of thousands of neutral mutations. The comparison of these variants is thus made easier and the likely causative mutations more efficiently identified.

What mutation causes what disease?

VariantMaster works by successive data filtering. If a child is affected with a genetic disease of unknown molecular cause, the comparison of DNA sequencing data from both parents and child, allows for the identification of a list of genetic mutations, that may explain the disease. The pro-gram takes into account the probability that the mutation is actually present in a family member, then, from this probability, identifies the mutations, which are only present in the affected individual.

The programme takes into account **the probability that the mutation appears in a family member**, then, from this probability, isolates the mutations which are only present in the affected individual

VariantMaster uses public databases, which collect (anonymous) sequenced genomes from many individuals, in order to identify which variants are frequent in the general population, and therefore not pathogenic (not disease-causing). The software selects only the patient's rare genetic variants, that are not found in these databases. It per¬forms the same comparisons and selections with data from family members. Next, the software will try to establish possible matches, between the few rare variants found in the affected individual but not in his family members, and known pathogenic mutations. The tests conducted on hundreds of samples by the Geneva team have therefore demonstrated that the program can iden¬tify causative mutation in families affected with various genetic conditions such as mental retardation, schizophrenia, primary ciliary dyskinesia and even certain types of cancers. In the case of cancer, the software detects oncogenic mutations - that promote the likelihood of developing cancer - by comparing the sequenced DNA of healthy cells with that of tumour cells in a per¬son with cancer. For example, for colorectal cancer, VariantMaster was able to identify the somatic mutations that caused the development of these tumours, thereby identifying the responsible genes.

The research group who developed VariantMaster will continue to test it by using this algorithm to identify the genetic variants lin¬ked to certain diseases, including schizophrenia and certain forms of leukaemia. The identification of the molecular cause of these di¬seases will indeed open up new therapeutic prospects and will be the key to more targeted therapies in personalized medicine.

contact

Federico A. Santoni
+41 78 314 92 63
federico.santoni@unige.ch

UNIVERSITÉ DE GENÈVE
Service de communication
24 rue du Général-Dufour
CH-1211 Genève 4

Tél. 022 379 77 17

media@unige.ch
www.unige.ch