Genetic diversity of enzymes alters metabolic individuality

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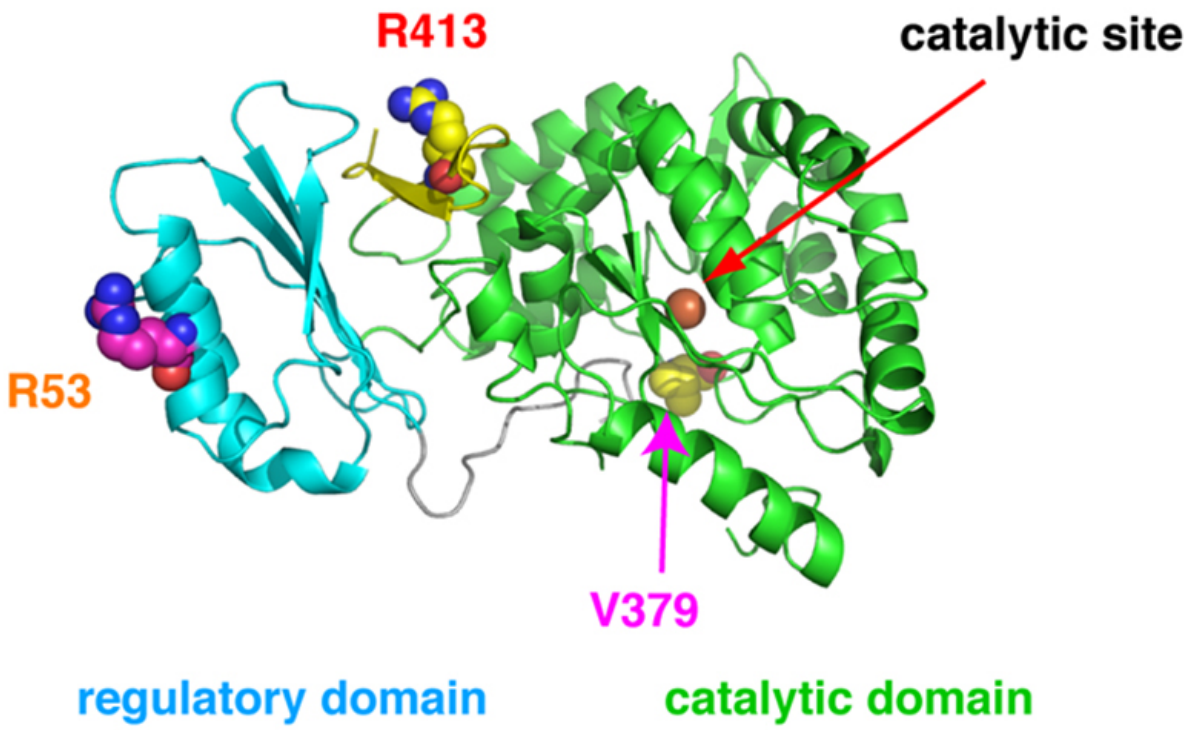

The metabolites in plasma were analyzed by NMR spectroscopy. Credit: Tohoku Medical Megabank Organization

Scientists from Tohoku University's Tohoku Medical Megabank Organization (ToMMo) have published research about genetic diversity and metabolome in *Scientific Reports*.

"We discovered genetic variants affecting enzymatic activities in healthy people," said Dr. Seizo Koshiba. "Our study shows that genetic polymorphisms, structural location of mutation and effect for phenotype correlate with each other in the human population. This implies that metabolic individuality and susceptibility for diseases are possibly resulted from the moderate variants and much more deleterious, but rare, variants."

In their analyses, researchers found the following results:

- The relationship between structural variants of enzymes and metabolic phenotypes in the human population was surveyed in the association study of metabolite concentrations with whole genome sequence analysis data.
- Five associations between metabolites and gene variants were identified. Four of the gene variants are known to be related to metabolic diseases. The residues substituted by these variants are located in peripheral regions of the catalytic sites or related regulatory domains of enzymes.
- Two people have larger changes of metabolite levels of phenylalanine. They had rare gene variants, which substitute residues located near the catalytic site.
- These data demonstrate that variant frequency, structural location and effect for phenotype correlate with each other in the human population.

ToMMo will study environmental and genetic influence on individual differences of proteomics and metabolomics. ToMMo aims to discover useful biomarkers for disease prevention and early diagnosis through the identification and quantification of metabolites in blood. Such studies can contribute to the advancement of personalized prevention and treatment of diseases, as well as the identification of disease mechanisms and development of new therapeutics.

These findings are based on the analysis of blood samples from 512 healthy people who participated in the Tohoku Medical Megabank Project Community-Based Cohort Study and the Birth and Three-Generation Cohort Study.

Some of the data can be found on ToMMo's website:

Japanese Multi Omics Reference Panel (jMorp) at https://jmorp.megabank.tohoku.ac.jp/.

More information: Seizo Koshiba et al, The structural origin of metabolic quantitative diversity, *Scientific Reports* (2016). DOI: 10.1038/srep31463

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