

Gene mutation causes chronic bad breath

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For the first time, researchers have uncovered that bad breath can be caused by a genetic defect. A mutation in the gene SELENBP1 leads to the absence of the protein that converts the sulphur compound methanethiol. Researchers from Radboud University and Radboud university medical center have published these findings in *Nature Genetics*.

Bad breath (halitosis) is usually caused by bacteria in the oral cavity that produce sulphur compounds. Little is known about other causes of [bad breath](#), but it has long been thought that it might also have a genetic cause. In the nineties, Dr. Albert Tangerman (Radboud university medical center, internal medicine) discovered a Dutch family with several members having bad breath.

Together with Professor of Inborn errors of Metabolism Ron Wevers, he looked for a cause. They came across sulphur compounds, including the foul-smelling methanethiol. This compound gives rise to a strong cabbage-like odour. "Methanethiol is produced in large amounts in the intestines, and can originate from food. We believed that the protein responsible for getting rid of methanethiol was defective in these patients", says Wevers, "however, we could not find a lead for this in their metabolism. The process by which the body counteracts this compound was unknown. So at that point we were stuck."

From bacterium to human

Wevers presented this problem at several conventions and as a result was

contacted by families from Germany and Portugal with the same problem. In addition, a collaboration with Microbiology Professor Huub Op den Camp, a specialist in sulphur conversion in bacteria, was established. Together with researchers from University of Warwick, they recently discovered a protein in the bacterium *Hyphomicrobium* that converts methanethiol: methanethiol oxidase.

The bacterium feeds on contamination in sewage, including sulphur compounds like methanethiol, removing them from the water.

The researchers then looked to see whether the gene encoding the methanethiol oxidase protein in the bacteria was also present in humans. The human gene that corresponded most closely was SELENBP1. Huub Op den Camp: But the function of the corresponding human protein SELENBP1 was unknown. This also meant we did not know which compounds our body converts methanethiol into. The gene SELENBP1 is reported in the literature to be involved in tumour suppression. However, we immediately hypothesized that the absence of this protein could be the cause of bad breath in these patients."

Widely distributed defect in metabolism

Wevers and Op den Camp investigated the breath, blood and urine of these patients, and found an increased amount of methanethiol and dimethyl sulphide. Wevers: "That was a direct clue that in these patients' metabolism an error occurs, leading to the accumulation of four sulphur compounds, including methanethiol, in their blood. Methanethiol and dimethyl sulphide are extremely volatile and are thus easily exhaled via the lungs. Because we had now identified the human protein converting methanethiol, SELENBP1, we looked at these patients' DNA. We found they all had mutations in the gene SELENBP1."

Further research produced more evidence for this new discovery. For

example, these patients' skin cells had significantly lower levels of the [protein](#) and showed little or no enzyme activity. This same pattern was found in knock-out mice. This led to the conclusion that SELENBP1 is indeed a methanethiol oxidase and that mutations in this gene cause chronic bad breath. This mutation might be more common than we think: the researchers calculated that about 1 in 90,000 people carry the mutation. No cure is available for these patients. For the present, they can reduce bad breath only by dietary measures. Further research will focus on the development of a possible therapy, and on the role of [compounds](#) deriving from methanethiol in a healthy metabolism.

More information: Arjan Pol et al. Mutations in SELENBP1, encoding a novel human methanethiol oxidase, cause extraoral halitosis, *Nature Genetics* (2017). [DOI: 10.1038/s41588-017-0006-7](https://doi.org/10.1038/s41588-017-0006-7)

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