# MicroRNA controls mammary gland development in mice

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Mammary gland tissue of milk-producing mice with (left) and without (right) miR-212/132: the consequences of the lack of the ribonucleic acid molecules are clear to see. The milk ducts (dark red) did not grow in the tissue without the microRNAs. Credit: Image: Max Planck Institute for Biophysical Chemistry

Hormones, growth factors and several proteins ensure that development occurs in the right way, at the right time. The components that cause breast development in mammals, for example, were thought to be largely known. However, as a team of scientists from Göttingen, Frankfurt and Hanover have now discovered, in the case of breast development, hormones and proteins do not account for the full story. The scientists have shown that tiny ribonucleic acid molecules play a key role in this process. The mammary glands of mice lacking the gene for the microRNAs 212 and 132 failed to grow at puberty. (*Nature Genetics*, Nov. 7, 2010)

The scientists have demonstrated for the first time in an animal model that small ribonucleic acid molecules, so-called microRNAs, also fulfil an important function in organ development. "This came as a surprise to us," says project leader Kamal Chowdhury from the Max Planck

Institute for Biophysical Chemistry in Göttingen. "The mice used in our experiments had all of the hormones, growth factors and proteins that ensure normal breast development. But the absence of the microRNAs miR-212 and miR-132 resulted in the complete failure of duct development in the mammary glands of mice."

It is well known that microRNAs perform very important regulatory functions inside living cells. Although they do not code for proteins, they are responsible for the fine-tuning of the production of certain proteins and intervene extensively in metabolic processes. The question is however: how does this activity shape the morphology of the whole organism? "Using various experiments, we were able to demonstrate that this RNA family plays a key role in mammary gland development and we could locate where these molecules presumably intervene on a regulatory basis," explains Chowdhury.

The mammary gland, which is also known as the milk gland, consists of the milk ducts and the surrounding connective tissue, which has a supportive and regulatory function. The connective tissue also appears to be the location where miR-212 and miR-132 are produced and intervene in the developmental process. Chowdhury and his colleague Ahmet Ucar were able to demonstrate with their experiments that this is the only place where the genes for these ribonucleic acid molecules are "switched on" in the breast tissue.

## Molecular dimmer

According to the researcher's model, the microRNA molecules appear to control the production of a protein called MMP-9. "The microRNAs can down-regulate the production of MMP-9, like a dimmer switch," explains Ucar. If the microRNAs are missing, more MMP-9 proteins are produced and they accumulate near the milk ducts. They appear to activate a signalling pathway there, which prevents the normal growth of

the milk ducts in the glandular tissue. "These tiny RNA molecules carry out their regulatory function by influencing the communication between the two tissues of the mammary gland," says Ucar. Other experiments now need to be carried out to examine whether these microRNAs also regulate breast development in humans. At the moment, the scientists can only speculate about what happens when the microRNAs do not function correctly. "Whether such malfunctions can lead to the formation of tumours, for example, is something that needs to be examined in further studies," says Chowdhury.

**More information:** Ahmet Ucar, Vida Vafaizadeh, Hubertus Jarry, Jan Fiedler, Petra A B Klemmt, Thomas Thum, Bernd Groner, and Kamal Chowdhury, "miR-212 and miR-132 are required for epithelial stromal interactions and mouse mammary gland development," *Nature Genetics*, advanced online publication, November 7, 2010

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