

## Know your product and your costumers

There are two things a good salesman should know about his products: What does it do? and Who is going to buy it? Now try to imagine a butcher, who thinks that an apple is just a fruit and windows are only for cleaning. Now this butcher is thinking about selling computers in his shop, simply because he has heard a lot of good things about computers and between all the different sausages, the minced meat and t-bone steaks there is still some space left in his counter. So he could easily fit in some laptops. It would be revolutionary and ground breaking, something no butcher has ever tried before. So what do computers and a butcher have to do with scientific research? It is very simple. In many ways I am like this butcher and the product I want to sell is a protein called "hey".

The butcher, despite not knowing much about computers, is quite a clever guy. He is aware that he needs to learn more about computers, before he can start selling them. So he walks along the street outside his butchery and looks where he can find computers. Maybe that will give him a hint. And he observes that the accountant across the street has one and there are computers in the bank, too. So he concludes that banks and accountants need computers. In my research lab we did the same, we looked where "hey" is present and we found it for example in the heart. That at least tells us where "hey" is located, but now we would like to know what it is needed for.

A simple way for the butcher to figure out why there are computers in the accountants office and in the bank would have been to simply ask. However we could not really ask the heart either why it needs "hey", so we and the butcher had to come up with another plan. During the night the butcher broke into the bank and the accountant's office and stole all their computers. Then he went to the roof of his shop with binoculars to see what would happen the next day. And that was very conclusive. In the bank there were angry people shouting complains, because they were given out wrong amounts of cash and the accountant got picked up by the police, because the numbers in his accounts were wrong and he was believed to be a fraud. So the butcher concluded computers are somehow needed for calculating.

With "hey" we essentially did the same. In my lab a special mouse was created which lacks the "hey" protein and in this mouse quite a few things went wrong. For example the wall separating the chambers of the heart was not formed correctly and growth of blood vessels was somehow impaired. In many cases the defects were so severe that the mice died. This way we could figure out that "hey" is crucial for developmental processes, like blood vessel formation and heart development.

Additional to removing "hey" we also did the opposite. We used mouse and human cells and tested what happens when we increase the amount of "hey" in these cells. Here we observed that depending on the amount of "hey" more or less copies from certain genes are made. Genes are basically manuals containing instructions on how to build proteins. They are copied, because this way the originals can be kept at a safe place, the nucleus. "Hey" seems to somehow regulate the copying process from certain genes. Thereby it changes the amount of protein made according to the instructions, because more copies mean that you can make more protein at the same time. We think that this is related to the defects observed in heart and in blood vessels. Maybe "hey" controls that the correct amounts of certain proteins are made, so that the correct cells in heart and blood vessels

are formed during development. Now we would really like to know, which proteins and corresponding genes these are.

The butcher found himself in a similar situation. After finding out all this information about computers, he should figure out who would potentially buy computers from him, apart from the accountant and the bank that just got raided. So he thought of another plan: He labelled the stolen computers with a special dye, which is invisible on the computers but sticks to human skin and turns green. Then he placed these labelled computers on the street with a sign saying: "computers for free". Some people passing by thought that this is an awesome opportunity and that they need a new computer. So not aware of the dye they took the computers home. Others were just complaining about the rubbish on the streets and went their way. The next day the butcher could see many people with green hands and he thought: "these must be my potential customers." However there were many different groups: students, doctors, web designer and many other more that had picked up a computer. He also got many false positives, because not everybody picking up a computer for free would also pay for one. So he got really confused.

In the lab we labelled our "hey" protein as well, which allowed us to track it to certain genes, it binds to. However the number of genes "hey" seems to bind is very high and we have also false positives, because not every gene bound by "hey" is necessarily regulated by it. This makes it really complicated to identify the most important ones, which could help us explain the defects in heart and blood vessels.

So up to today the butcher and I are still trying to figure out which potential customers/ genes are the most important ones.

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