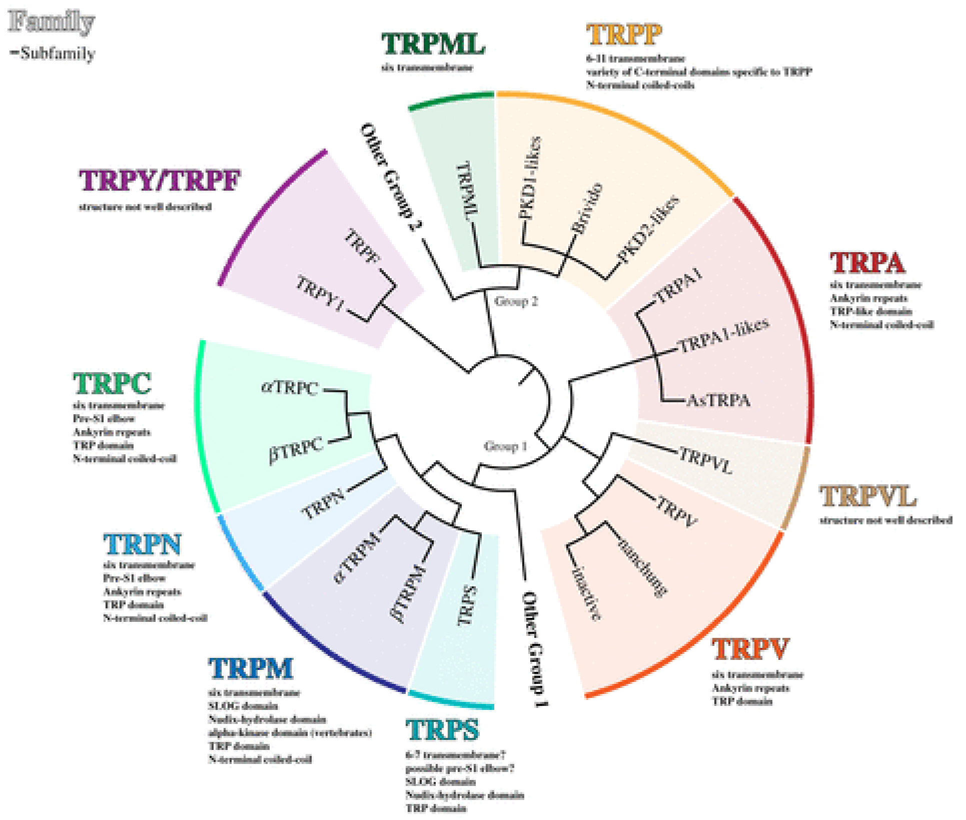
The Nobel Prize in Medicine or Physiology 2021 to David Julius and related work at KTH Royal Institute of Technology by Erik Fransén

David Julius is one of the two winners of this year's Nobel Prize in Medicine or Physiology. He has studied how our senses to perceive heat and cold work. How can our brain get information about our surroundings or of our skin temperature? The answer is that there are nerve pathways that run from the brain all the way to the skin. In the finest nerve fibers at the far end, in the skin, there are specialized receptors (sensory organs) which are affected by temperature. In the nerve fiber skin (envelope), there are special proteins (molecules) that change depending on the temperature. These proteins open a channel in the envelope of the nerve cell for ions to pass in or out of the nerve cell. For the heat-sensitive proteins, the ion flow increases when it gets warmer and for the cold-sensitive proteins when it gets colder. The ion flow leads to the nerve cell sending its nerve impulse. It is passed on through the entire chain of nerves from the skin, to the spinal cord, then on up to the brain (cerebrum). This creates your experience of heat or cold.

The ion channels that David Julius discovered are members of a whole family of ion channels called TRP channels (transient receptor potential channels). They got their name from the channel found in the fly Drosofila. So far, 6 main types have been found in mammals and many more in other organisms. The channels that react to heat are called TRPV1 and are thus a member of the V-family and the one that reacts to cold is called TRPM8 and is a member of the M-family.



The reason why spicy food that contains, for example, pepper are perceived as hot is that the TRPV1 channel gets its sensitivity to heat upregulated by a substance in pepper called capsaicin. In the same way, the TRPM8 channel gets its sensitivity to cold upregulated by menthol. TRP channels are not only sensitive to heat or cold, but also to other signals. It can be acidity (pH), chemical substances that are dangerous or mechanical stretching of the skin. Many of the channels respond to several of these signals, but to a slightly different degree.

TRP channels are not only found in sensory cells but they are found in several parts of the nervous system in many different types of nerve cells. Given the sensitivity of the TRP channels to various stimuli, one may ask what they have to do in the middle of the brain at all? The answer is that they respond to chemical signals that the brain itself creates. With their unique ability to sense signals, it seems that they sometimes act as a kind of “exchange office”, they sense one type of signal and translate it into another type of signal and become like linguistic translators who translates one type of chemical signal to another so that different parts of the nerve cell's chemistry can "talk" to each other.

We at KTH have studied how they can be involved in working memory. The ion channels we have studied belong to the TRPC family. They thus belong to the C family and are considered to be the most typical of the TRP channels. They respond not only to the electrical voltage of the nerve cell but at the same time to signals of calcium ions. It is the fact that they need two simultaneous signals that we believe makes them contribute to the role of the nerve cell in working memory. In addition, this channel has the property that it can provide a relatively long-term response (several seconds). We believe that this can give the nerve cell its own kind of "memory". The nerve impulses that the nerve cell receives from its neighbors do not subside so quickly, but their effect remains longer and thus can affect the activity of the nerve cell for a longer period of time.

Now one might think that there is a long way between an individual nerve cell and the ability we have to remember things for a short time, and of course it is. The brain is a system of many brain centers and each center has many different types of nerve cells and working memory is an ability that comes from a collaboration between several centers. At the same time, you can remind yourself of what a cup of coffee does to us in the morning (not to mention what happens if we drink coffee in the evening). We become alert and our brains work better. Why? Coffee contains caffeine and the caffeine blocks the activity of a receptor called the adenosine receptor. To make a long story short, one can see that a molecule (caffeine) can affect a receptor that affects nerve cells and in the end we feel refreshed and can think better. Similarly, we propose that TRPC channels affect nerve cells so that they can affect the activity of a brain center called the entorinal cortex so that it ultimately provides us with better working memory. Our experimental studies have been published in the well-known journal Nature and the models we have made at KTH have been published in e.g. the journals Neuron and the Journal of Neuroscience.

If you want to know more about TRP channels or about our research, contact me at erikf@kth.se
Thanks for reading.

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