Laudation for Dr. Maurice Michel

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Winner of the Eppendorf Award for Young European Investigators 2023

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Enzymes are marvels of evolution that are essential for life. They are catalysts that lower the activation energy barrier and allow chemical reactions to run smoothly which otherwise would never proceed in aqueous solutions at ambient temperature. In addition, and at least as important, they define which of the many possible chemical reactions on their substrate does take place. Consider a molecule as simple as the sugar glucose: You can hydrolyze it, esterify it, oxidize it, and more, and this at different positions in the molecule. Indeed, enzymes acting on the same substrate are highly specific for only one type of reaction, which is defined by the structure of their catalytic center.

A lot of work has been invested in controlling enzyme activities with small molecules or drugs. To inhibit an enzyme, one strategy is to develop a molecule that disguises as the biological substrate, enters the catalytic center and then gets stuck or does something nasty so that the enzyme is rendered non-functional. Some enzymes can also be activated by small molecules but this usually requires tweaking of the enzyme away from the catalytic center, bending or distorting it so that it can interact with the substrate more efficiently.

What I have been telling you so far is standard knowledge, developed and refined over many years, and taught in introductory courses of biochemistry. However, sometimes an odd observation contradicts established concepts. In most cases, it is correctly dismissed as an artefact, but there is a slight chance that you miss a major discovery unless you are sufficiently open-minded to follow it through. This is what Maurice Michel has done, the winner of this years' Eppendorf Young Investigator Award whom I will now introduce to you.

Maurice Michel is from Germany. He studied Chemistry at a small engineering university in Germany (Clausthal-Zellerfeld, rather close to where I live) and then joined the lab of Peter Seeberger, a renowned chemist working on biomolecules, for both his Masters and PhD thesis. Here he became familiar with bioorganic chemistry and worked on the synthesis of glycosylated membrane lipids in the parasite Trypanosoma. For his postdoc, he chose the laboratory of Thomas Helleday at the Karolinska Institutet in Stockholm, where he has remained to assume the position of Assistant professor.

In the Helleday lab, Maurice was assigned to a project involving an enzyme needed for repairing DNA damaged by oxygen, termed 8-oxoguanine-DNA glycosylase. Although we all need oxygen for life, it is a rather aggressive molecule, and all living organisms need to cope with oxidative damage of biomolecules. DNA is particularly vulnerable, with oxidative damage causing mutations that are conducive for cancer development. No surprise that enzymes involved in DNA repair are of high interest, and the Helleday laboratory had already a sophisticated toolkit available for studying the enzyme, including compound libraries to manipulate the enzyme.

Maurice then came up with an odd finding: He found an activator that seemed to bind to the catalytic center of the protein – defying common experience. Apparently, no one in the lab was particularly interested, but he had the freedom to follow up his "crazy" ideas. What he found in the end amounts to a major discovery: Not only was the small molecule capable of activating the enzyme but also of enticing it to catalyze a second reaction, thus operating as an organic catalyst, a concept that just a few years ago had won the Nobel Prize to Benjamin List and Dave MacMillan. The findings have profound implications and open an entirely new field.