

The DNA is well known for its role as our genetic storage molecule. Interestingly, like many proteins and RNAs, it can also catalyze chemical reactions as an enzyme, for which it has to abandon the double helical conformation, in which we are used to picturing it. Catalytic DNA molecules, also called deoxyribozymes, have never been found in nature. Scientists prepare them by producing a large number of individual synthetic DNA strands and then selecting those that are able to catalyze reactions. DNA catalysts can be used, for instance, for cutting RNA molecules at a particular position, or to link two of them. One of the applications they may find in the future is to target genes that are involved in particular diseases.

Although these molecules are known since more than two decades ago, little progress has been made in their application to industrial processes, medicine or nanotechnology. The reason behind this is that we know very little about the way they work, which is fundamental in order to create more efficient DNA catalysts. How DNA catalysts work can only be explained on the basis of their structure, and it was only recently that the first structure of a catalytic DNA molecule was determined with atomic accuracy. Besides, DNA catalysts have never been classified in such a way that their study was made easier; which in contrast has been done for proteins and RNAs in many different ways. These are the reasons for the existing gap in understanding how DNA catalysts work, in comparison to how well RNA and protein catalysis are understood.

In order to bridge this gap I propose to classify all the discovered DNA catalysts based on their sequence, structure and function. Just as for RNA and proteins, from this classification, we will learn what a particular group of DNAzymes share in common. In addition, we will determine the atomic structure of some DNA catalysts, which will explain how they work and, simultaneously, allow the rational re-design of these molecules to transform them into more efficient tools. Last, we will develop a database that will ensure open access to the ever growing knowledge of DNA catalysts, their structure, function, relevant applications and chemical properties. This database will support an international community of users, among which, scientists from different fields be motivated to find out which are established or new applications for which DNA enzymes have the greatest potential.

Altogether, the results of this work are expected to reveal currently unknown features of DNAzymes, which will enable further studies on their structure and function. The knowledge generated during this project will motivate the use and spur the development of deoxyribozymes as research tools, providing a low-cost and highly customizable alternative to other existing tools. More importantly, the discovery of consensus sequences within a family of DNA catalysts, will enable the identification of catalytic-like DNA sequences among natural DNAs, bringing us a step closer to answering an intriguing evolutionary question concerning the existence of DNA catalysts in nature.