The little things in life that keep us healthy: Producing a chromatin remodeling machine in the test tube

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Our cells usually contain copies of our genetic information that is stored inside the so-called nucleus, a small compartment of the cell. In order to fit the genetic information into this confined space, our genetic material, the DNA, is packaged into a special "complex" made up of the DNA and a number of proteins. The resulting packaged version of our genetic information inside the nucleus is called chromatin.

Chromatin can have a rather complex architecture, but at the most basic level, it is made up of small building blocks called nucleosomes. These are in turn composed of specialized proteins called histones around which a short piece of DNA is wrapped. DNA that is located within a nucleosome, i.e. wrapped around histone proteins, is typically less accessible to the cellular machinery that reads the genetic information stored in our DNA. For this reason, the packaging state of chromatin needs to be dynamically changed in order to make genes accessible at the right time and the right location. One way that this can be achieved is by "moving" nucleosomes, the building blocks of chromatin, back-and-forth on the DNA, thereby changing which portions of the DNA are accessible and which ones cannot be read because they are tucked away inside a nucleosome.

Chromatin remodelers are cellular machines or enzymes that can do precisely this: they can move about nucleosomes and shift their position on the DNA. As such, remodelers play a key role in determining which genes are active. Not surprisingly, whether remodelers are "on" or "off", needs to be tightly controlled. If this is not the case, severe human diseases such as cancer and development disorders are often the consequence. Despite this importance, how these chromatin remodelers are switched "on" and "off" is not very well understood.

Here, we set out to produce a chromatin remodelling machine in our laboratory. In order to achieve this, we programmed cultured cells to produce the desired protein. We then developed a procedure that allowed us to purify the desired protein by removing all other unwanted cellular proteins. We also characterized the purity and basic properties of the purified protein using a number of biochemical and biophysical approaches. These experiments allowed us to conclude that the produced chromatin remodeler is highly pure and well-behaved in solution.

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