In living organisms, the genetic information is encoded on long DNA molecules that are tightly packed inside the nucleus. There exist specialized proteins that associate with DNA and compress it so that it can be squeezed on such a tiny space. The same proteins help to unwind DNA when the genetic code has to be read out - for replication or transcription. Some regions of the DNA however, have to remain inactive and then proteins prevent the message to be revealed. Heterochromatin protein 1a is a molecule involved in all of these processes and is present in a wide range of organisms ranging from yeast to human. It helps to compress DNA but also to keep genes silent. Even though we know how this protein looks like, that is how the atoms constituting it are connected to each other, the mechanism of DNA regulation is not fully understood. We believe that to understand this process one has to focus not only on a single structure but on the way how protein structure changes with time. These structural rearrangements, that are caused by interactions with other molecules in a cell, determine how HP1a molecules binds to DNA. Since protein molecules and atoms are extremely small, one has to develop methodologies in order to spy them.

My goal is to use the nuclear magnetic resonance spectroscopy (NMR), a method which allows one to observe molecular motions, that is how the shape of protein molecule changes with time while they exert their biological function. This complements the static pictures provided by other experimental technics. Structural plasticity helps to better fulfill physiological roles by interacting with numerous binding partners or enabling catalyzis of chemical reactions in a living cell. I strongly believe, that understanding of the conformational changes that occur during recognition of the activating proteins or DNA molecules would enable us to understand how a single protein HP1a can be involved in such a large variety of DNA related processes. The NMR spectroscopy is based on the interaction of protein molecules with the electromagnetic field in a so called NMR spectrometer. One can apply series of the electromagnetic pulses and deduce about the shape and motions of a protein sample. Two modern high-field NMR spectrometers are located in our laboratory at the Biological and Chemical Research Centre of the University of Warsaw. Their use in conjunction with innovative isotope labelling schemes that allows one to introduce such non-radioactive isotopes as deuterium or ^{13}C into the protein structure, enables quantitative studies of large protein complexes, including HP1a.

The first step of my research will be the production of the samples containing human HP1a and its activators. I will make use of the genetically modified non-pathogenic *E. coli* cells to produce large quantities of human proteins. Significant part of this grant proposal budget will cover growing media and the isotopes used for protein expression. Subsequently, I will separate my proteins of interest from all other *E. coli* proteins with so called chromatography methods. Proteins, purified in this way, will be the object of the NMR study.

High novelty of this project relies on the fact that it combines modern NMR with the innovative deuterium labelling strategies. This enables us to study large protein objects, rarely accessed by NMR. This multidisciplinary project, that crosses the borders of biology, chemistry and physics, has the major goal of providing valuable information about physiologically relevant processes occurring in every single cell of a human body. This information may be used in a future to design new therapeutic strategies. On the other hand, the new NMR methodologies that I plan to develop, would help scientists to get insights into the structure-function-dynamics relationship for other protein systems involved in many different biological processes.