Description for the general public

Calcium Pyrophosphate Dihydrate Deposition (CPPD) disease is an ailment related to age. It manifests itself with microscopic crystals in a synovial fluid in joints. It can cause rheumatoid arthritis and osteoarthritis. In the United States of America it affects half of the population over 85 years old and in Italy, it was the 4th most prevalent musculoskeletal condition. In severe cases, when the knee joint is affected it causes immobilization of a patient. Acute CPPD crystal arthritis is treated symptomatically by local application of ice-packs and joint aspiration. In severe cases joint replacements are being applied.

CPPD related diseases are thought to be one of the most common under-recognized conditions causing joint pain, osteoarthritis, rheumatoid arthritis and acute neck pain. The main component of a crystal, pyrophosphate is a molecule that is a product of DNA/RNA polymerization. Its levels are being maintained at low level by the ubiquitous enzymes called pyrophosphatases. In joints of people with CPPD, these enzymes are malfunctioning allowing crystals to grow.

In this project we will use phage display strategy to search for new compounds which could be use to treat CPPD. By mimicking, in artificial conditions, the process of evolution we want to obtain short, up to ten amino acid long, peptides that possess the power to utilize pyrophosphate from the surface of CPPD-related crystal. We will start from a random peptide sequence enriched in residues that are crucial for catalytic properties of pyrophosphatases and we will clone them into the bacteriophagal (bacterial virus) gene coding its coat proteins the way that our sequence is going to be displayed on the virus particle surface. During proliferation in their natural hosts, E. coli cells, we will allow viruses to mutate giving us a variety of different peptides. Subsequently, we will select only these bacteriophages able to bind to a pyrophosphate and dissolve the CPP crystal. The best performing sequences are going to be chosen for the next round of mutation - a second generation. We will repeat the experiment until we obtain the peptide with desired properties. Subsequently, we will perform enzymatic assays and three-dimensional study in order to elucidate the mechanism of our peptide actions.
In the end, we hope that our peptide could be used in ointments or intra-articular injections, becoming the very first therapeutic drug against CPPD.