The interaction of iron ions with the heat shock protein B1 Scientific

objective:

The aim of the project is to understand the interaction of iron ions with the heat shock protein B1 (HSPB1) involved in ferroptosis, iron-dependent regulated cell death.

Justification:

The HSPB1 protein is capable of inhibiting the process of ferroptosis by hindering the transport of iron into the cell and thereby reducing its concentration inside the cell. In the amino acid sequence of HSPB1 we found the same motif as is present in ferritin, the iron-storing protein, i.e. HEERE in ferritin and HEERQ in HSPB1. Therefore, there was the hypothesis that HSPB1 may not only indirectly reduce the amount of iron in the cell by inhibiting the transport, but it is very likely that it can bind iron ions directly, which has not yet been studied. The middle Glu (E) residue of the HE**E**RE motif from ferritin is involved in the binding of two iron ions, and the residues His and Cys, also present in the HSPB1 structure, are known for their iron binding capacity, therefore these fragments are potential iron binding sites.

The planned studies will check the interaction of iron ions with selected peptide fragments of HSPB1 protein and with the whole protein.

The research results will contribute to the broadening of knowledge about ferroptosis and the role of HSPB1 in this process. The possibility of using this knowledge includes developing new strategies for treating cancer, because elevated levels of HSPB1 and iron have been found in cancer cells. Lowering their HSPB1 levels could lead to the initiation of ferroptosis and the destruction of the cell. In turn, in diseases in which ferroptosis plays a pathogenic role, such as Huntington's disease or acute kidney damage, it could be possible to strengthen the protective role of HSPB1.

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