

Title: Piezolytes and osmolytes in the circulatory system - roles in health and disease.

Research project objectives/Research hypothesis

We hypothesize that piezolytes and osmolytes play an important role in the circulatory system and that accumulation of those molecules in organism may be a protective mechanism for the heart and other organs. We speculate that cardiovascular diseases such as hypertension (high blood pressure) and heart failure (e.g. after myocardial infarction) may be associated with changes in concentration of those molecules in tissues. Our hypothesis is based on the following facts.

Piezolytes and osmolytes are small molecules that protect proteins against high hydrostatic and osmotic pressures, respectively. The importance of piezolytes and osmolytes has been recognized in marine animals which are exposed to high hydrostatic stress (deep water) and osmotic stress (salty water). However, the knowledge on the role of osmolytes and piezolytes in mammals is scant. Finally, some of mammalian tissues are also exposed to hydrostatic and osmotic stress e.g. the heart (beat-to-beat change in blood pressure inside the heart) or red blood cells that go to the kidneys (inner part of the kidney is 3-4-fold "more salty" than systemic blood). Importantly, those osmotic and hydrostatic stresses are significantly augmented in cardiovascular diseases such as hypertension and heart failure.

Research project methodology

We will evaluate:

1. physiological concentrations of piezolytes and osmolytes in blood and tissues in mice, rat and guinea pigs.
2. the concentration of osmolytes and piezolytes in blood and tissues in animal models of human cardiovascular diseases such as hypertension and heart failure,
3. the effect of factors increasing the risk of cardiovascular diseases such as high-salt diet, high-fat diet, ethanol, nicotine and the effect of factors decreasing the risk such as blood pressure lowering-drugs and lipid-lowering drugs,
4. the effect of treatment with piezolytes and osmolytes on the development of hypertension and heart failure in animal models of human cardiovascular diseases,
5. the effect of osmolytes and piezolytes on proteins that build cells of the heart and other tissues.

Expected impact of the research project

Despite a significant progress in diagnosis and treatment, the mortality due to cardiovascular diseases is very high. Recent decades are characterized by a rapid growth of interventional cardiology but a little progress in prevention and pharmacological treatment. This partially results from significant gaps in the knowledge on physiological and pathological processes occurring in the circulatory system.

The knowledge on the role of osmolytes and piezolytes in the circulatory system in mammals is lacking. Results of our study will broaden the knowledge on the function of piezolytes and osmolytes in health and disease.

The findings of the project may be important for developing preventive (e.g. dietary) and pharmacological strategies for cardiovascular diseases.