

DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Chronic kidney disease (CKD) is a complex systemic disturbance. CKD occurs when the nephrons are damaged or destroyed and is associated with the accumulation of toxins in the body. CKD is a serious public health problem affecting 12-15% of the world population; the prevalence of CKD in the population aged 65 and older is estimated to be between 25% and 35%. The disturbances in bone metabolism in patients with CKD are very common and may lead to morbidity, mortality, increased risk of fractures, and decreased quality of life.

Recent studies indicate that serotonin, often called the hormone of happiness, may play a key role in controlling bone metabolism. Serotonin is produced in our body from an essential amino acid, called tryptophan. It is estimated that only 1% of tryptophan is used for serotonin synthesis; about 95% of tryptophan is metabolized via the kynurenine pathway. Although, there are many indications that kynurenine pathway may play a key role in CKD development, the associations between kynurenine pathway and disturbances in bone metabolism in CKD patients are unknown.

The aim of this project is to understand the association between tryptophan and its metabolite via kynurenine pathway (kynurenine and 3-hydroxykynurenine) and biomechanical properties of bone as well as bone metabolism in experimental model of chronic renal failure in rats. Undoubtedly, the comprehensive analysis of association between tryptophan, kynurenine and 3-hydroxykynurenine concentrations and bone metabolism is completely new look at osteoporosis in CKD patients.

The project will allow for a comprehensive analysis of mechanisms involved in disturbances of mineral and bone metabolism in CKD. We will analyze the biomechanical properties of bones and assess bone remodeling by measurement of serum bone turnover biomarkers. Furthermore, we will evaluate the calcium-phosphate metabolism including calcitropic hormones involved in its regulation. We will also determine tryptophan, kynurenine and 3-hydroxykynurenine in rat serum, brain and bone tissue homogenates using high performance liquid chromatography. Additionally, we will evaluate genes expression of enzymes implicated in tryptophan metabolism via kynurenine pathway. Finally, we will investigate the association between tryptophan and tryptophan metabolite levels in rat serum, brain and bone tissue homogenates and biomechanical parameters or bone turnover biomarkers in rats with chronic renal failure.

The current project will combine the integrated techniques of biomechanics, molecular biology, biochemistry, analytical chemistry and biostatistics. It will provide new data on bone metabolism in patients with CKD. The proposed experiments may contribute to the development of new strategies for the diagnosis, treatment, and prevention of osteoporosis in CKD patients.