Role of the C-type Natriuretic Peptide in the development of the vascular phenotype in Marfan disease.

Background. Marfan Syndrome (MFS) is an autosomal dominant inherited connective tissue disorder affecting the cardio-vascular system. Aortic dissections and ruptures are the primary cause of morbidity and mortality in these patients. No treatment really cures patients.
The C-type natriuretic peptide (CNP) is a local regulator of skeletal growth and of vascular homeostasis, remodeling and angiogenesis. CNP is constitutively released by endothelial cells, whereas TGF beta (increased in Marfan patients) stimulates its secretion by smooth muscle cells.

The aim of this project is to determine whether altered CNP signaling pathway contributes to the development of the vascular phenotype in MFS.

Methodology. Plasma and vessel biopsies will be taken **from Marfan patients** (RAVAD registery, CHUV Lausanne.). In parallel, experiments will also be performed on **Fbn1** $^{C1041G/+}$ **mouse model** which recapitulates several of the human phenotypes, including aortic wall degeneration and aneurysm development.
The objectives of the project are to: 1) **determine** whether CNP secretion is altered in the plasma and locally in the vessels during the development of the Marfan syndrome. The expression of its receptors, NPR-B and NPR-C, will also be investigated during the development of MFS. 2) **identify** the cells responsible for altered CNP signaling pathway and **3) identify** the cellular dysfunctions linked to altered CNP signaling pathway.4) **rescue** the phenotype by regulating CNP levels.

Potential Significance. The results generated in project will help to understand the role of the CNP-mediated signaling pathway in the development of MFS. They will open the door to new therapies and will generate great hope for patients.