CURRICULUM VITAE - PROF. ANTONIO ROSSI
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Prof. Antonio Rossi has a long-standing interest in biochemical and molecular studies of heritable skeletal disorders caused by defects in proteoglycan metabolism and in collagen structure.

In particular starting from 1994, Dr. A. Rossi has been involved, in collaboration with Prof. A. Superti-Furga (Kinderspital Zurich, Zurich) and Dr. J. Bonaventure (Hopital Necker, Paris), in biochemical and molecular studies of the diastrophic dysplasia "family" of disorders caused by mutations in the diastrophic dysplasia sulfate transporter (DTDST) gene encoding for a sulfate transporter crucial for sulfate uptake and proteoglycan sulfation. In order to get new insight in the pathogenesis of DTDST disorders and to develop pharmacological therapies of diastrophic dysplasia he has generated the first mouse strain (dtd mouse) with a mutation in the Dtdst gene resulting in a skeletal phenotype which reproduces at the clinical, morphological and biochemical level human diastrophic dysplasia. The new knowledge on the molecular basis of DTDST disorders gained from the dtd mouse has suggested a potential pharmacological therapy with cysteine derivatives (i.e. acetylcysteine) as source of sulphate for macromolecular sulfation.

Recent scientific activity and key achievements in the last 10 years:
He has recently demonstrated that newborn dtd mice from pregnant females treated for the whole pregnancy with acetylcysteine show a skeletal phenotype amelioration both at the morphological, biochemical and histological level. Further studies targeted at the treatment of dtd mice after birth have demonstrated the same phenotypic amelioration in the first 3 weeks of age. Both studies have provided proof of principle data of the drug efficacy.
Based on these results, negotiations are ongoing with a pharmaceutical company and some clinical centers (USA, Australia, Finland, Switzerland) in order to start a clinical trial in patients with diastrophic dysplasia and recessive multiple epiphyseal dysplasia.

In collaboration with prof. V. Cormier- Daire (Hopital Necker, Paris) using cultured skin fibroblasts from patients with Desbuquois dysplasia type 1, he has demonstrated reduced synthesis of glycosaminoglycan chains when cells are incubated with ß-xyloside, a compound that enhances glycosaminoglycan synthesis providing the first evidence that CANT1 is involved in proteoglycan metabolism. Based on these results he has generated the first Cant1 knock-in and knock-out mouse which are actively studied in order to get new insight on the role of Cant1 in the skeleton. Using the animal models, he has demonstrated that Cant1 mutation affects not only GAG synthesis, but also GAG length, sulfation and proteoglycan secretion in the extracellular matrix. Moreover, the defect cause ER enlargement that is not linked to conventional ER stress and the activation of the UPR.

In collaboration with prof. A. Superti-Furga (University of Lausanne), he has collaborated at the identification of the first IMPAD1 mutations in patients with chondrodysplasia gPAPP type. Moreover, in collaboration with Polygene (Rumlang, Switzerland), he has generated an Impad1 knock-in mouse model of this disorder using a Cre-mediated genetic switch. By deep phenotyping of the model, he has demonstrated that this conditional strategy should be considered cautiously because the generation of alternative splicing could affect the phenotype.

Furthermore due to his interest in the field of skeletal disorders caused by defects in proteoglycan metabolism, he has been involved:
i) in collaboration with prof. A. Superti-Furga in recessive Larsen Syndrome and Humero-Spinal Dysostosis. He has focused on the effect of carbohydrate sulfotransferase 3 (CHST3) deficiency on newly synthesized fibroblast proteoglycans and on the enzyme activity in fibroblasts cell lysates from the patients.
ii) in collaboration with prof. U. Kornak (Charitè, Berlin) in the study of glycosaminoglycan (GAG) properties in a mouse model of gerodermia osteodysplastica (caused by mutations in the GORAB gene).
iii) in collaboration with prof. T. Schinke (University of Hamburg) in urine GAG analysis in a mouse model of mucopolysaccharidosis type VI (caused by mutation in ARSB gene).
iv) in collaboration with prof. L. Garavelli (Dept. Medical Genetics, Reggio Emilia Hospital) and A. Superti-Furga in the field of linkeropaties, disorders caused by defects in the enzymes involved in the synthesis of the tetrasaccharide linker region of proteoglycans, he has performed biochemical studies of patients with mutations in the B4GALT7 and B3GALT6 genes (encoding for galactosyltransferase I and II respectively).

Prof. A. Rossi was president of the Italian Society for the Study of Connective Tissues (SISC) from 2011 to 2016.
He was delegate of the University of Pavia at the Italian Biotechnology Consortium (CIB, http://www.cibiotech.it/) from 2011 to 2016.
He is member of the SIB (Italian Society of Biochemistry and Molecular Biology), SISC (Italian Society for the Study of Connective Tissues) and of the ISDS (International Skeletal Dysplasia Society).