BIOGRAPHICAL SKETCH

NAME: Antonio Rossi

POSITION TITLE: Associate professor in Biochemistry

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pavia, Pavia	Master degree in Biology	July 1985	
University of Pavia, Pavia	PhD in Biochemistry	Nov 1988- Nov 1991	Biochemical studies in Osteogenesis Imperfecta
University of Pavia, Pavia	Post-doc	Jan1992-Nov 1994	Biochemical studies on heritable connective tissue disorders
Kinderspital Zurich, Zurich, prof A. Superti-Furga Lab	Research training	Aug 1995-Oct 1997	Research training from August 1995 to October 1997 on mutation screening and proteoglycan sulfation in the SLC26A2 family of chondrodysplasia

A. Personal Statement

(Here you can insert a short description of your professional status and achievements. Max 10 lines)

Prof. Antonio Rossi has a long-standing interest in biochemical and molecular studies of heritable skeletal disorders affecting cartilage and bone. His research is focused on the use of murine models of skeletal dysplasias caused by defects in proteoglycan biosynthesis and sulfation. In particular, he has generated and characterized a mouse model of diastrophic dysplasia, a chondrodyspalsia caused by defects in proteoglycan sulfation. At present this in vivo model is used in order to develop pharmacological therapies by a drug repositioning approach. He has also focused on Desbuquois dysplasia type 1, a chondrodysplasia caused by defects in glycosaminoglycan synthesis. In order to get new insight on the molecular basis of the disorder he has generated and validated a knock-out and knock-in mouse model. In the field of skeletal dysplasia involving bone, he has also collaborated to the deep phenotyping of animal models (mouse and zebrafish) of Osteogenesis Imperfecta (OI) a group of skeletal disorder caused by defects in collagen type I.

B. Positions and Honors

Positions and Employment

Dec. 1994-Sept. 2001 Researcher at the Department of Biochemistry, University of Pavia, Pavia.
From Oct. 2001 Associate Professor in Biochemistry at the University of Pavia, Pavia

Honors

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 Italian Society of Biochemistry and Molecular Biology (SIB), Italian Society for the Study of Connective Tissues (SISC) and of the International Skeletal Dysplasia Society (ISDS).

Reviewer Experience

He has acted as reviewer for several international journals in the Biochemistry and Molecular Biology field.

C. Contributions to Science

1. Development of a drug repositioning approach to diastrophic dysplasia

He has 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. In view of a potential clinical trial, recently he has focused on the identification of potential non-invasive biomarkers that can be used to follow the efficacy of the treatment. He has recently demonstrated that urinary glycosaminoglycan sulfation analysis from the patients is a reliable biomarker to follow a pharmacological treatment targeted at increasing proteoglycan sulfation.

2. Characterization of a mouse model of Desbuquois dysplasia

He has generated the first Cant1 knock-in and knock-out mouse in order to get new insight on the role of Cant1 in skeletal development and homeostasis. Using the murine strains, he has confirmed results on patient fibroblasts that Cant1 impairment cause defects in GAG synthesis. He has demonstrated that the GAG synthesis defect led to the synthesis and secretion of proteoglycans with shorter GAG chains compared with wild-type animals. However, this alteration has not resulted in the synthesis and secretion of decorin and aggrecan in the unglycanated form. Moreover, the defect cause ER enlargement that is not linked to conventional ER stress and the activation of the UPR. The mouse strains have been validated as animal models of Desbuquois dyspalsia type 1.

3. Due to his interest in the field of skeletal disorders caused by defects in proteoglycan metabolism, he has collaborated to the study of: Desbuquois dyspalsia type 1 (with prof V. Cormier-Daire, Imagine Institute Paris), recessive Larsen Syndrome and Humero-Spinal Dysostosis (with prof A. Superti-Furga, University of Lausanne), gerodermia osteodysplastica (with prof U. Kornak, Charitè Berlin), mucopolysaccharidosis type VI (with prof. T. Schinke, University of Hamburg) and linkeropaties, disorders caused by defects in the enzymes involved in the synthesis of the tetrasaccharide linker region of proteoglycans (with prof L. Garavelli Dept. Medical Genetics, Reggio Emilia Hospital and A. Superti-Furga, University of Lausanne).

4. Skeletal disorders caused by type I collagen defects.

In the field of skeletal dysplasias involving bone, he has also collaborated to the deep phenotyping of animal models (mouse and zebrafish) of Osteogenesis Imperfecta (OI) a group of skeletal disorders caused by structural defects in collagen type I or in proteins important for collagen synthesis and post-translational modifications. In particular Zebrafish mutants have been studied as models not only to get insight on the molecular basis of OI but also to test specific pharmacological treatments.

Publications:

1. N-acetylcysteine treatment ameliorates the skeletal phenotype of a mouse model of diastrophic dysplasia.

Monti L, Paganini C, Lecci S, De Leonardis F, Hay E, Cohen-Solal M, Villani S, Superti-Furga A, Tenni R, Forlino A, Rossi A. Hum Mol Genet. 2015 Oct 1;24(19):5570-80. doi: 10.1093/hmg/ddv289.

2. FGF signalling regulates bone growth through autophagy.
Cinque L, Forrester A, Bartolomeo R, Svelto M, Venditti R, Montefusco S, Polishchuk E, Nusco E, Rossi A, Medina DL, Polishchuk R, De Matteis MA, Settembre C.
Nature. 2015 Dec 10; 528: 272-275. doi: 10.1038/nature16063.

3. NANS-mediated synthesis of sialic acid is required for brain and skeletal development.
van Karnebeek CD, Bonafé L, Wen XY, Tarailo-Graovac M, Balzano S, Royer-Bertrand B, Ashikov A, Garavelli L, Mammi I, Turolla L, Breen C, Donnai D, Cormier V, Heron D, Nishimura G, Uchikawa S, Campos-Xavier B, Rossi A, Hennet T, Brand-Arzamendi K, Rozmus J, Harshman K, Stevenson BJ, Girardi E, Superti-Furga G, Dewan T, Collingridge A, Halparin J, Ross CJ, Van Allen MI, Rossi A, Engelke UF, Kluijtmans LA, van der Heeft E, Renkema H, de Brouwer A, Huijben K, Zijlstra F, Heisse T, Boltje T, Wasserman WW, Rivolta C, Unger S, Lefeber DJ, Wevers RA, Superti-Furga A.
Nat Genet. 2016 Jul;48(7):777-84. doi: 10.1038/ng.3578.

4. The chaperone activity of 4PBA ameliorates the skeletal phenotype of Chihuahua, a zebrafish model for dominant osteogenesis imperfecta.
Gioia R, Tonelli F, Ceppi I, Biggiogera M, Leikin S, Fisher S, Tenedini E, Yorgan TA, Schinke T, Tian K, Schwartz JM, Forte F, Wagener R, Villani S, Rossi A, Forlino A.
Hum Mol Genet. 2017, Aug:26(15):2897-2911. doi: 10.1093/hmg/ddx171.

5. Polyethylene Glycol-Poly-Lactide-co-Glycolide Block Copolymer-Based Nanoparticles as a Potential Tool for Off-Label Use of N-Acetylcysteine in the Treatment of Diastrophic Dysplasia.
Chiesa E, Monti L, Paganini C, Dorati R, Conti B, Modena T, Rossi A, Genta I.
J Pharm Sci. 2017 Dec;106(12):3631-3641. doi: 10.1016/j.xphs.2017.08.004.

6. 4-PBA ameliorates cellular homeostasis in fibroblasts from osteogenesis imperfecta patients by enhancing autophagy and stimulating protein secretion.
Besio R, Iula G, Garibaldi N, Cipolla L, Sabbioneda S, Biggiogera M, Marini JC, Rossi A, Forlino A.
Biochim Biophys Acta. 2018 Feb 10;1864(5 Pt A):1642-1652. doi: 10.1016/j.bbadis.2018.02.002.

7. The Lysosomal Protein Arylsulfatase B Is a Key Enzyme Involved in Skeletal Turnover.
Pohl S, Angermann A, Jeschke A, Hendrickx G, Yorgan TA, Makrypidi-Fraune G, Steigert A, Kuehn SC, Rolvien T, Schweizer M, Koehne T, Neven M, Winter O, Velho RV, Albers J, Streichert T, Pestka JM, Baldauf C, Breyer S, Stuecker R, Muschol N, Cox TM, Saftig P, Paganini C, Rossi A, Amling M, Braulke T, Schinke T.
J Bone Miner Res. 2018 Dec;33(12):2186-2201. doi: 10.1002/jbmr.3563.

8. Impaired proteoglycan glycosylation, elevated TGF-β signaling, and abnormal osteoblast differentiation as the basis for bone fragility in a mouse model for gerodermia osteodysplastica.
Chan WL, Steiner M, Witkos T, Egerer J, Busse B, Mizumoto S, Pestka JM, Zhang H, Hausser I, Khayal LA, Ott CE, Kolanczyk M, Willie B, Schinke T, Paganini C, Rossi A, Sugahara K, Amling M, Knaus P, Chan D, Lowe M, Mundlos S, Kornak U.
PLoS Genet. 2018 Mar 21;14(3):e1007242. doi:10.1371/journal.pgen.1007242.

9. Calcium activated nucleotidase 1 (CANT1) is critical for glycosaminoglycan biosynthesis in cartilage and endochondral ossification.
Paganini C, Monti L, Costantini R, Besio R, Lecci S, Biggiogera M, Tian K, Schwartz JM, Huber C, Cormier-Daire V, Gibson BG, Pirog KA, Forlino A, Rossi A.
Matrix Biol. 2019 Aug;81:70-90. doi: 10.1016/j.matbio.2018.11.002. Epub 2018 Nov 12.
PMID: 30439444

10. Testing the Cre-mediated genetic switch for the generation of conditional knock-in mice.
Capulli M, Costantini R, Sonntag S, Maurizi A, Paganini C, Monti L, Forlino A, Shmerling D, Teti A, Rossi A.
PLoS One. 2019 Mar 13;14(3):e0213660. doi: 10.1371/journal.pone.0213660. eCollection 2019. PMID: 30865697

11. Cellular stress due to impairment of collagen prolyl hydroxylation complex is rescued by the chaperone 4-phenylbutyrate.
Besio R, Garibaldi N, Leoni L, Cipolla L, Sabbioneda S, Biggiogera M, Mottes M, Aglan M, Otaify GA, Temtamy SA, Rossi A, Forlino A.
Dis Model Mech. 2019 Jun 20;12(6). pii: dmm038521. doi: 10.1242/dmm.038521. PMID: 31171565

12. Bone and connective tissue disorders caused by defects in glycosaminoglycan biosynthesis: a panoramic view.
Paganini C, Costantini R, Superti-Furga A, Rossi A.
FEBS J. 2019 Aug;286(15):3008-3032. doi: 10.1111/febs.14984. Epub 2019 Jul 25. Review. PMID: 31286677

13. Severe Peripheral Joint Laxity is a Distinctive Clinical Feature of Spondylodysplastic-Ehlers-Danlos Syndrome (EDS)-B4GALT7 and Spondylodysplastic-EDS-B3GALT6.
Caraffi SG, Maini I, Ivanovski I, Pollazzon M, Giangiobbe S, Valli M, Rossi A, Sassi S, Faccioli S, Rocco MD, Magnani C, Campos-Xavier B, Unger S, Superti-Furga A, Garavelli L.
Genes (Basel). 2019 Oct 12;10(10). pii: E799. doi: 10.3390/genes10100799.

14. Enzyme replacement therapy in mice lacking arylsulfatase B targets bone-remodeling cells, but not chondrocytes.
Hendrickx G, Danyukova T, Baranowsky A, Rolvien T, Angermann A, Schweizer M, Keller J, Schröder J, Meyer-Schwesinger C, Muschol N, Paganini C, Rossi A, Amling M, Pohl S, Schinke T.
Hum Mol Genet. 2020 Mar 27;29(5):803-816. doi: 10.1093/hmg/ddaa006.

15. Improvement of the skeletal phenotype in a mouse model of diastrophic dysplasia after postnatal treatment with N-acetylcysteine.
Paganini C, Gramegna Tota C, Monti L, Monti I, Maurizi A, Capulli M, Bourmaud M, Teti A, Cohen-Solal M, Villani S, Forlino A, Superti-Furga A, Rossi A.
Biochem Pharmacol. 2021 Mar;185:114452. doi: 10.1016/j.bcp.2021.114452.

16. Phenotypic Characterization of Immortalized Chondrocytes from a Desbuquois Dysplasia Type 1 Mouse Model: A Tool for Studying Defects in Glycosaminoglycan Biosynthesis.
Gramegna Tota C, Valenti B, Forlino A, Rossi A, Paganini C.
Int J Mol Sci. 2021 Aug 27;22(17):9304. doi: 10.3390/ijms22179304.
PMID: 34502207

17. Targeting cellular stress in vitro improves osteoblast homeostasis, matrix collagen content and mineralization in two murine models of osteogenesis imperfecta.
Garibaldi N, Contento BM, Babini G, Morini J, Siciliani S, Biggiogera M, Raspanti M, Marini JC, Rossi A, Forlino A, Besio R.
Matrix Biol. 2021 Apr;98:1-20. doi: 10.1016/j.matbio.2021.03.001. Epub 2021 Mar 31.
PMID: 33798677

18. Biallelic variants in SLC35B2 cause a novel chondrodysplasia with hypomyelinating leukodystrophy.
Guasto A, Dubail J, Aguilera-Albesa S, Paganini C, Vanhulle C, Haouari W, Gorría-Redondo N, Aznal-Sainz E, Boddaert N, Planas-Serra L, Schlüter A, Vélez-Santamaría V, Verdura E, Bruneel A, Rossi A, Huber C, Pujol A, Cormier-Daire V.
Brain. 2022 Oct 21;145(10):3711-3722. doi: 10.1093/brain/awac110. PMID: 35325049

19. Biallelic variants in the SLC13A1 sulfate transporter gene cause hyposulfatemia with a mild spondylo-epi-metaphyseal dysplasia.
van de Kamp JM, Bökenkamp A, Smith DEC, Wamelink MMC, Jansen EEW, Struys EA, Waisfisz Q, Verkleij M, Hartmann MF, Wang R, Wudy SA, Paganini C, Rossi A, Finken MJJ.

Clin Genet. 2023 Jan;103(1):45-52. doi: 10.1111/cge.14239. Epub 2022 Oct 3. PMID: 36175384

20. Identification of potential non-invasive biomarkers in diastrophic dysplasia.
Paganini C, Carroll RS, Gramegna Tota C, Schelhaas AJ, Leone A, Duker AL, O'Connell DA, Coghlan RF, Johnstone B, Ferreira CR, Peressini S, Albertini R, Forlino A, Bonafé L, Campos-Xavier AB, Superti-Furga A, Zankl A, Rossi A, Bober MB.
Bone. 2023 Oct;175:116838. doi: 10.1016/j.bone.2023.116838. Epub 2023 Jul 16.
PMID: 37454964

21. Cell differentiation and matrix organization are differentially affected during bone formation in osteogenesis imperfecta zebrafish models with different genetic defects impacting collagen type I structure.
Daponte V, Tonelli F, Masiero C, Syx D, Exbrayat-Héritier C, Biggiogera M, Willaert A, Rossi A, Coucke PJ, Ruggiero F, Forlino A.
Matrix Biol. 2023 Aug;121:105-126. doi: 10.1016/j.matbio.2023.06.003. Epub 2023 Jun 17.
PMID: 37336269

22. CaMKII inhibition due to TRIC-B loss-of-function dysregulates SMAD signaling in osteogenesis imperfecta.
Besio R, Contento BM, Garibaldi N, Filibian M, Sonntag S, Shmerling D, Tonelli F, Biggiogera M, Brini M, Salmaso A, Jovanovic M, Marini JC, Rossi A, Forlino A.
Matrix Biol. 2023 Jun;120:43-59. doi: 10.1016/j.matbio.2023.05.002. Epub 2023 May 11.
PMID: 37178987

23. Cant1 Affects Cartilage Proteoglycan Properties: Aggrecan and Decorin Characterization in a Mouse Model of Desbuquois Dysplasia Type 1. Gramegna Tota C, Leone A, Khan A, Forlino A, Rossi A, Paganini C.
Biomolecules. 2024 Aug 26;14(9):1064. doi: 10.3390/biom14091064.
PMID: 39334831

24. The administration of exogenous HSP47 as a collagen specific therapeutic approach.Besio R, Garibaldi N, Sala A, Tonelli F, Aresi C, Maffioli E, Casali C, Torriani C, Biggiogera M, Villani S, Rossi A, Tedeschi G, Forlino A.
JCI Insight. 2025 Feb 6:e181570. doi: 10.1172/jci.insight.181570. Online ahead of print.
PMID: 39913197

25. Combined antiresorptive and new anabolic drug approach in osteogenesis imperfecta zebrafish models.
Masiero C, Tonelli F, Aresi C, Filibian M, Larionova D, Cotti S, Doria F, Torriani C, Bertuccio P, Odone A, Villani S, Rossi A, Witten PE, Forlino A.
JBMR Plus. 2025 Jul 2;9(9):ziaf112. doi: 10.1093/jbmrpl/ziaf112. eCollection 2025 Sep.
PMID: 40823439

D. Past and Ongoing Research Support

Main research projects as PI:

PI Telethon grant n. D.83: A mouse model of diastrophic dysplasia to test potential therapies of the disorder. (1999, 3 years)

PI Telethon grant n. GGP06076: The role of proteoglycan sulfation in skeletal development and maintenance: an in vivo approach with a mouse model of diastrophic dysplasia. (2006, 3 years).

PI Telethon grant n. GGP11079: The functional role of the Calcium Activated Nucleotidase 1 (CANT1) gene in the skeleton: an in vivo study with a mouse model of Desbuquois Dysplasia. (2011, 3 years).

PI Exploratory Telethon grant n. GEP15062: Chondrodysplasia with joint dislocations gPAPP type: insight on the molecular basis of the disorder and the role of IMPAD1 in post-natal skeletal development (2016, 1 year).

PI “Fondazione Cariplo” grant: A proteomic approach for the diagnosis and therapy of skeletal disorders. (2006, 2 years).

Partner of a Strategic European Research Project (STREP) on the "Pathophysiology of the cartilage growth plate" (FP6, “EuroGrow” project, LSHM-CT-2007-037471) (2007, 3 years).

Partner in the European research project FP7-HEALTH 2013 Innovation 1 “Systems Biology for the functional validation of genetic determinants of skeletal diseases” grant agreement n. 602300 (SYBIL) (2013, 5 years).

Coordinator and PI of a PRIN project, PRIN 2003: Development of new therapies with in vitro and in vivo models of connective tissue disorders.

Coordinator and PI of a PRIN project, PRIN 2009: The role of sulfation in proteoglycan metabolism and in skeletal development and homeostasis in vivo.

PI of a PRIN research Unit, PRIN 2015: New experimental therapies for genetic skeletal diseases.

Coordinator and PI of a PRIN project, PRIN 2022: Characterization of skeletal disorders linked to proteoglycan defects as a tool to get new insight on the molecular basis of glycosaminoglycan synthesis

E. Experience as a research supervisor

6 postdocs

11 PhD students

Several Bachelor or Master students in Biology or Medical Biotechnology