

ALLEGATO A

UNIVERSITÀ DEGLI STUDI DI MILANO

Procedura di selezione per la chiamata a professore di II fascia da ricoprire ai sensi dell'art. 18, commi 1 e 4, della Legge n. 240/2010 per il settore concorsuale 05/E2 BIOLOGIA MOLECOLARE ,

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Giovanni Sorrentino

CURRICULUM VITAE

INFORMAZIONI PERSONALI (NON INSERIRE INDIRIZZO PRIVATO E TELEFONO FISSO O CELLULARE)

COGNOME	SORRENTINO
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RESEARCH KEYWORDS

Cancer; Metabolism; Multipotent stem cells; Bioengineering; High-content screening; Drug repositioning; p53; YAP/Hippo pathway; Mevalonate pathway; Synthetic hydrogels; Liver and Intestinal organoids; Bile acids.

RESEARCH EXPERIENCE

2017 – 2020

FEBS long-term postdoctoral fellow | Laboratory of Metabolic Signaling, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Lead and supervision of the following projects (Advisors: Prof. Kristina Schoonjans; Prof. Matthias Lutolf):

- Mechano-modulatory synthetic niches for liver organoid-based clinical application (published in *Nature Communications*).
- Dissecting the role of bile acids and TGR5 signaling in adult intestinal stem cells homeostasis (published in *Gastroenterology*).

2015 – 2017

Italian Foundation for Cancer Research (FIRC) postdoctoral fellow | National Laboratory CIB, Trieste, Italy

Lead and supervision of the following projects (Advisor: Prof. Giannino Del Sal):

- Dissecting the crosstalk between lipid biosynthesis and mechanotransduction (published in *Nature Communication* as corresponding author).
- Investigation of the role of mechanical cues in controlling mutant p53 stability and gain-of-functions (published in *Nature Cell Biology*).
- Identification of novel hormonal YAP/TAZ regulators by high-content screening (published in *Nature Communications*).
- Identification of a crosstalk between YAP and mutant p53 proteins involved in cancer cell proliferation (published in *EMBO reports*).
- Development of bioinformatic tools for the identification of pharmacogenomics association between cancer mutations and drug sensitivity (published in *Oncotarget and Nucleic Acid Research*).

2011 – 2014

Phd Student | University of Trieste, Trieste, Italy

Lead and supervision of the following project (Advisor: Prof. Giannino Del Sal):

- Identification a novel crosstalk between YAP/TAZ and cellular metabolism (published in *Nature Cell Biology*)

2009 – 2011

Graduate research fellow | National Laboratory CIB, Trieste, Italy

Lead and supervision of the following project (Advisor: Prof. Giannino Del Sal):

- Identification of the Prolyl-isomerase Pin1 as a key regulator of p53 mitochondrial translocation (published in *Cell Death and Differentiation*)

2007 – 2008

Graduate research assistant | University of Ferrara, Ferrara, Italy

Lead and supervision of the following project (Advisors: Prof. Rosario Rizzuto; Prof. Paolo Pinton):

- Using Aequorin to study mitochondrial calcium homeostasis (*published in BMC cell biology*).

EDUCATION

2014

University of Trieste | Trieste, Italy

PhD: Molecular Biomedicine

Supervisor: Prof. Giannino Del Sal

Thesis title: Metabolic control of YAP/TAZ by the mevalonate pathway

2008

University of Ferrara | Ferrara, Italy

MSc: Medical-Pharmaceutical Biotechnology, *magna cum laude*

2005

University of Ferrara | Ferrara, Italy

BSc: Biotechnology, *magna cum laude*

TEACHING EXPERIENCE

- Supervisor of a Ph.D. candidate (Doctoral program in Biotechnology and Bioengineering; École Polytechnique Fédérale de Lausanne).
- Supervisor of three Ph.D. candidates (Doctoral program in Molecular Biomedicine) and two master degree interns (University of Trieste).
- Teaching assistant, Molecular oncology master degree course, lectures on "Cancer Metabolism" (University of Trieste).

ACADEMIC QUALIFICATION

Italian academic qualification as associate professor (Abilitazione Scientifica Nazionale) in: Biochemistry 05/E1; Molecular Biology 05/E2; Experimental Biology 05/F1; Pathology 06/A2.

RESEARCH SUMMARY

One of my most important scientific achievements has been providing the first evidence, and then dissecting the underlying mechanisms, of a metabolic layer of control of the mechanotransducers YAP/TAZ. In another study, I have described a mechanism by which stress hormones promote YAP activation and breast cancer progression via mechanical remodeling of the tumor microenvironment. In a recent publication, I have discovered that activation of the metabolic mevalonate pathway controls mutant p53 stability and gain of functions by altering cell mechanoperception and stiffness. Finally, I have very recently unveiled an unexpected link between the physical properties of the ECM and lipid metabolism, which strongly affects stem cell specification.

My current research is instead aimed at understanding the fundamental principles that regulate intestinal and liver stem cell homeostasis and at studying how metabolic pathways and the physical microenvironment integrate each other to control these processes, with the ultimate goal of translating this knowledge for regenerative medicine therapies. To address these basic biomedical questions, I am adopting integrative approaches combining dietary induced and genetically engineered mouse models, tissue engineering as well as 3D organotypic cultures (intestinal and liver organoids).

Thus, my previous and current research has focused at dissecting, at multiple levels, the complex and still largely unexplored interplay between cell metabolism and mechanotransduction in the context of cancer and adult stem cell niches.

In my future research I envision to integrate my expertise in the fields of cancer, stem cells and bioengineering to generate cutting edge research lines aimed at understanding the basic principle of

tumor initiation and development as well as at defining novel strategies for stem cell-mediated regenerative therapies in order to establish innovative pharmacological approaches.

AWARDS AND FELLOWSHIPS

- Best oral presentation award: "A bioinspired synthetic niche enables culture of liver organoids suitable for clinical application"; "12th LIMNA Symposium", Lausanne, 2019.
- Selected by the Council for the Lindau Nobel Laureate Meetings to participate at the "68th Lindau Nobel Laureate Meeting", 2018.
- Recipient of a three years FEBS long-term Fellowship, 2017.
- "Chiara D'Onofrio Junior Award" from Italian Society for Biophysics and Molecular Biology, 2014.
- Recipient of the two years postdoc FIRC (Fondazione Italiana per la Ricerca sul Cancro) Fellowship "Anita Sambo", 2014.
- Best poster award, Karolinska Institutet Summer School on Targeted Cancer Therapies, 2013 Stockholm.

CONFERENCE PRESENTATION

- A bioinspired synthetic niche enables culture of liver organoids suitable for clinical application. Oral presentation delivered at "44th FEBS congress", Krakow 2019.
- A bioinspired synthetic niche enables culture of liver organoids suitable for clinical application. Oral presentation delivered at "12th LIMNA Symposium", Lausanne 2019.
- Identification of novel YAP/TAZ kinases regulated by metabolism. Poster presentation delivered at AACR "Metabolism and Cancer" meeting, Seattle 2015.
- Metabolic control of YAP/TAZ by the mevalonate pathway. Oral presentation delivered at "Cancer Stem Cells" EMBO workshop, Catanzaro 2014.
- Metabolic control of YAP/TAZ by the mevalonate pathway. Oral presentation delivered at SIBBM (Italian Society for Biophysics and Molecular Biology), Trento 2014.
- Metabolic control of YAP/TAZ by the mevalonate pathway. Oral presentation delivered at "Dangerous Liaisons" SIC (Italian Society for Cancerology) meeting, Ferrara 2014.
- Pin1 activates the mitochondrial death program of p53. Poster presentation delivered at 5th mutant p53 workshop, Ariccia 2011.
- Pin1 activates the mitochondrial death program of p53. Poster presentation delivered at 36th FEBS congress, Turin 2011.

EDITORIAL EXPERIENCE

Review activity for high-impact scientific journals (Cell, Science, Nature, Nature Cell Biology, EMBO journal, Cell Death and Differentiation, Oncogene, PNAS, Cell Metabolism) as post-doc in Giannino Del Sal's laboratory and Kristina Schoonjans's laboratory. Reviewer editor for Frontiers in Oncology from 2016. Reviewer for Cellular Physiology and Biochemistry from 2016.

CLINICAL TRIALS

Two publications by Dr. Sorrentino (Sorrentino et al. 2014 and Ingallina, Sorrentino et al. 2018) provided the evidence-based rational for the design and activation of two clinical phase II studies i) on the

activity of pre-operative zoledronate in triple negative breast cancer (clinical trials.gov NCT02347163) and ii) a multicenter, randomized, phase II study of neoadjuvant chemotherapy associated or not with zoledronate and atorvastatin in triple negative breast cancers (clinical trials.gov NCT03358017).

PATENTS

European patent PC19177445 "Three dimensional models of tissue fibrosis", submission number 7524647, 29 May 2019.

MEMBERSHIPS

- Young Member of the Italian Society of Biochemistry and Molecular Biology (SIB) since 2016.
- Young Member of the Italian Society for Biophysics and Molecular Biology (SIBBM) since 2014.

REFERENCES

- Prof. Giannino Del Sal, Head of Molecular Oncology, National Laboratory CIB, Area Science Park Padriciano, 99 Trieste 34149, Italy +39 040375680; mailto: gdelasal@units.it
- Prof. Kristina Schoonjans, Laboratory of Metabolic Signaling, Institute of Bioengineering Ecole Polytechnique Federale de Lausanne, 1015 Lausanne, Switzerland; Secr: +41 21 693 95 22; mailto: kristina.schoonjans@epfl.ch
- Prof. Stefano Piccolo, University of Padova, Dept. Molecular Medicine, Via Ugo Bassi, 58 35131 Padova, Italy 0039 049 8276079; mailto: piccolo@bio.unipd.it

PUBLICATIONS

Corresponding author:

- **Sterol Regulatory Element Binding Protein 1 couples mechanical cues and lipid metabolism (2019).**
Bertolio R., Napoletano F., Mano M., Maurer-Stroh S., Fantuz M., Biciato S., **Sorrentino G.*** and Del Sal G*.
(*Nature Communications*). PMID: 30902980. *Corresponding authors.

First author:

- **Mechano-modulatory synthetic niches for liver organoid derivation (2020).**
Giovanni Sorrentino*, Saba Rezakhani*, Ece Yildiz, Sandro Nuciforo, Markus H. Heim, Matthias P. Lutolf § and Kristina Schoonjans§.
(*Nature Communications*). PMID: 32651372.
* equal contribution, §corresponding authors.

- **Bile Acids Signal via TGR5 to Activate Intestinal Stem Cells and Epithelial Regeneration (2020).**
Giovanni Sorrentino, Alessia Perino, Ece Yildiz, Gaby El Alam, Maroun Bou Sleiman and Kristina Schoonjans.
(*Gastroenterology*). PMID: 32485177.
- **The stiff RhoAd from mevalonate to mutant p53 (2018).**
Sorrentino G., Mantovani F. and Del Sal G.
(*Cell Death and Differentiation*). PMID: 29511341.
- **Mechanical cues control mutant p53 stability through a mevalonate–RhoA axis (2018).**
Ingallina E.*, **Sorrentino G.***, Bertolio R, Lisek K., Zannini A., Azzolin L., Severino L.U., Scaini D., Mano M., Mantovani F., Rosato A., Biciato S., Piccolo S. and Del Sal G.
(*Nature Cell Biology*). PMID: 29255172. *equal contribution
- **Glucocorticoid Receptor signalling activates YAP in breast cancer (2017).**
Sorrentino G.*, Ruggeri N.*, Zannini A., Ingallina E., Mano M., Biciato S. and Del Sal G.
(*Nature Communications*). PMID: 28102225. *equal contribution
- **YAP enhances the pro-proliferative transcriptional activity of mutant p53 proteins (2015).**
Di Agostino S.*, **Sorrentino G.***, Ingallina E., Valenti F., Ferraiuolo M., Biciato S., Piazza S., Strano S., Del Sal G.§ and Blandino G.§
(*EMBO reports*). PMID: 26691213. *equal contribution
- **MDP, a database linking drug response data to genomic information, identifies dasatinib and statins as a combinatorial strategy to inhibit YAP/TAZ in cancer cells (2015).**
Taccioli C.*, **Sorrentino G.***, Zannini A., Caroli J., Beneventano D., Anderlucci L., Lolli M., Biciato S§. and Del Sal G§.
(*Oncotarget*). PMID: 26513174. *equal contribution
- **p53 orchestrates calcium signaling in vivo (2015).**
Sorrentino G., Comel A., Del Sal G.
(*Cell Cycle*). PMID: 25880696.
- **Regulation of mitochondrial apoptosis by Pin1 in cancer and neurodegeneration (2014).**
Sorrentino, G.*, Comel, A.*, Mantovani, F., and Del Sal, G.
(*Mitochondrion*). PMID: 25132079. *equal contribution.
- **The cytoplasmic side of p53's oncosuppressive activities (2014).**
Comel, A.*, **Sorrentino, G.***, Capaci, V., and Del Sal, G.
(*FEBS Letters*). PMID: 24747877. *equal contribution.
- **Metabolic control of YAP and TAZ by the mevalonate pathway (2014).**
Sorrentino, G., Ruggeri, N., Specchia, V., Cordenonsi, M., Mano, M., Dupont, S., Piazza, S., Rosato A., Piccolo S. and Del Sal G.
(*Nature Cell Biology*). PMID: 24658687.
- **The prolyl-isomerase Pin1 activates the mitochondrial death program of p53 (2013).**
Sorrentino, G., Mioni, M., Giorgi, C., Ruggeri, N., Pinton, P., Moll, U., Mantovani, F., and Del Sal, G.
(*Cell Death and Differentiation*). PMID: 22935610.

Contributing author:

- **L-cell differentiation is induced by bile acids through paracrine serotonin signalling (2020).**
Mari Lilith Lund, **Giovanni Sorrentino**, Kristoffer Lihme Egerod, Chantal Kroone, Brynjulf Mortensen, Filip Krag Knop, Frank Reimann, Fiona M. Gribble, Daniel J. Drucker, Eelco J.P. de Koning, Kristina Schoonjans, Fredrik Bäckhed, Thue W. Schwartz, Natalia Petersen. (*Diabetes*).

- **GDA, a web-based tool for Genomics and Drugs integrated analysis (2018).** Caroli J., **Sorrentino G.**, Forcato M., Del Sal G., Biciato S. (*Nucleic Acid research*). PMID: 29800349
- **Stearoyl-CoA-desaturase 1 regulates lung cancer stemness via stabilization and nuclear localization of YAP/TAZ (2017).** Noto A., De Vitis C., Pisanu ME., Roscilli G., Ricci G., Catizone A., **Sorrentino G.**, Chianese G., Tagliatela-Scafati O., Triscioglio D., Del Bufalo D., Di Martile M., Di Napoli A., Ruco L., Costantini S., Jakopin Z., Budillon A., Melino G., Del Sal G5., Ciliberto G., Mancini R. (*Oncogene*). PMID: 28628115.
- **p53 at the endoplasmic reticulum regulates apoptosis in a Ca²⁺-dependent manner (2015).** Giorgi C., Bonora M., **Sorrentino G.**, Missiroli S., Poletti F., Suski J.M., Galindo Ramirez F., Rizzuto R., Di Virgilio F., Zito E., Pandolfi P.P., Wieckowski M.R., Mammano F., Del Sal G., Pinton P. (*PNAS*). PMID: 25624484.
- **Prolyl-isomerase Pin1 controls normal and cancer stem cells of the breast (2014).** Rustighi, A., Zannini, A., Tiberi, L., Sommaggio, R., Piazza, S., **Sorrentino, G.**, Nuzzo, S., Tuscano, A., Eterno, V., Benvenuti, F., et al. (*EMBO Mol Med*). PMID: 24357640.
- **Translocation of signalling proteins to the plasma membrane revealed by a new bioluminescent procedure (2011).** Giorgi, C., Romagnoli, A., Agnoletto, C., Bergamelli, L., **Sorrentino, G.**, Brini, M., Pozzan, T., Meldolesi, J., Pinton, P., and Rizzuto, R. (*BMC Cell Biol*). PMID: 21658234.

Data

12/07/2020

Luogo

Saint Sulpice