### Giulio Superti-Furga

CEO and Scientific Director CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences

Professor for Medical Systems Biology Medical University of Vienna

Scientific Director
Ri.MED Foundation Palermo Sicily

1987-1991: PhD in Molecular Biology at University of Zürich with M: Busslinger (Zürich,

Genentech, Inc. South San Francisco, and at the IMP Vienna)

1981-1986: MSc Molecular Biology Univ. Zürich (M. Busslinger, M. Birnstiel, C. Weissmann)

1968-1981: German School of Milan

#### Working experience:

2023-; Scientific Director Ri.MED Foundation, Palermo, Sicily, Italy

2005-: Director and CEO CeMM – Res. Center for Molecular Medicine of the ÖAW

2014-: Professor of Medical Systems Biology, Medical University of Vienna

2017-2019 Member of the Scientific Council of the ERC (European Research Council) 2005-2013: Guest Professor of Molecular Pharmacology, Medical University of Vienna 2000-2004: Scientific Director and Founder, Cellzome AG, Heidelberg and Cambridge

1997-2000: Guest Professor for Molecular Biology, University of Bologna

1993-2004: Staff Scientist/Team Leader European Molecular Biology Laboratory (EMBL) 1991-1993: PostDoc (EMBO/EU Fellow) EMBL Heidelberg (G. Draetta, S. Courtneidge)

#### Main other responsibilities:

- Boards (current): Exscientia (Oxford UK), Proxygen (Vienna, Austria), Human Technopole (Milan, Italy), Cancer Res. Institute Oslo University Hospital (Oslo, Norway)
- Vice Chair and designated Chair EU-Life (eu-life.eu)
- Boards and Committees (past, selection): Scientific Council of the European Research Council (2017 2019), Board of the University of Vienna (Universitätsrat), Institute for Research in Biomedicine (IRB Barcelona), Genome Austria (chair), Chemical Biology Consortium Sweden (Stockholm), EMBL Alumni Association (chair), ERC evaluation panel, Chair Evaluation Board VIB Ghent, International Agency for Cancer Research (Lyon), HSR San Raffaele (Milan), Virtual Liver Network (BMBF), Standing Technical Evaluation Committee of Lombardy Region for Research Funds (Milan), Harvard Armenise Foundation Fellowship Committee (Rome), Helmholtz Alliance on Systems Biology, Committee awarding the FEBS Letters Young Group Leader Prize (chair), Jubilee Fund City of Vienna, Ignaz L. Lieben Prize, Erwin Schrödinger Prize, Otto Mauer Prize.

# Awards, Memberships, Lectureship, ERC:

Faculty of 1000 (2004-2010)

European Molecular Biology Organization (2005)

Austrian Academy of Science (corresponding member 2007, full member 2010)

German National Academy of Sciences Leopoldina (2008) Officer (Ufficiale) Order of Merit of the Republic of Italy (2009)

ERC (European Research Council) Advanced Investigator Grant (2009) "i-FIVE"

Karl Landsteiner Prize of the Austrian Society for Immunology and Allergology (2009)

Science Prize City of Vienna (2011)

Austrian of the Year for the category Science (2011)

European Academy of Cancer Studies (2012)

ERC Proof of Concept Grants (2012, 2016)

Academia Europea (2014)

ERC Advanced Investigator Grant (2016) "Game of Gates"

Commander (Commendatore), Order of Merit of the Republic of Italy (2017)

Schrödinger Lecturer, Trinity College Dublin (2023)

Bard Lecturer, John Hopkins School of Medicine (2024)

**Publications:** > 270 papers (Pubmed), of which ~ 20 as senior or co-senior author in

*Nature*, *Science*, *Cell* and > 30 in *Nature*-sister journals cited > 50,000 times according to Google Scholar, h = 103

Top paper cited > 6,000 times

**Commercialization:** > 50 Patents (Lens), co-founder of five biotech companies: Cellzome

AG/Inc. Heidelberg and Cambridge (2000), Haplogen GmbH, Vienna (2010), Allcyte GmbH, Vienna (2016), Proxygen GmbH, Vienna (2020).

Solgate GmbH, Vienna (2020). Many partnerships with industry (Novartis, Pfizer, Boehringer Ingelheim). Winner GSK Drug Discovery Fast Track Challenge (2014), leader of EU Innovative Medicine Initiative Program "RESOLUTE" (2018) and "RESOLUTION" (2020).

**Conferences:** Co-organized > 40 conferences, 5 lecture series, speaker at > 150.

Building organizations: Built two highly successful research organizations from scratch to

> 150 people: 1. Cellzome GmbH and Inc. in Heidelberg and Cambridge, (1999-2004), sold to GSK and 2. CeMM (2005-present), developed into the premier medical research center of Austria, with

average IF per paper of >10 and unusually high degree of internal

collaborations

Science, Art, Society: Intensive advising and career mentoring of young investigators ; co-

founder of EU-Life, a consortium of European research centers to support European research excellence (NKI, FMI, Inst. Curie, etc.); work package leader H2020 EU project to unify innovative efforts to achieve gender equality in academia; co-founder GenomAustria, a citizen science/educational project and first genome project in a German speaking country; originator of EMBL Archive concept and inaugurated it 2018; proponent of three major projects at the interface between art and science: Brain Lounge, Time Capsule, CeMM Façade; organizer of SMART (Science, Medicine, Art, Research, Technology) Lecture and Landsteiner Lecture series for lay audience. Invented and organized "Utopia Institute of Research" Literary Contest with *Nature* in 2023.

### Major research projects:

# • Structure/function analysis of key proteins in cancer, immunology and metabolism:

Regulation of cancer tyrosine kinases and innate immunity receptors. Identified basic regulatory mechanisms of cytoplasmic tyrosine kinases, in particular elucidated unexpected intramolecular interactions of Src superfamily of kinases thereby contributing to solving the structure of Src, Abl and several BCR-ABL portions. Identified AIM2, IFIT1/3, TASL and their mechanism of action. Characterized new RAS regulator LZTR1. Currently we are working on key regulators of RAS and transporter proteostasis using genetics and new regulators of metabolic switch (OxPhos vs glycolysis). 1992-2012 EMBL, CeMM (various grants).

Hantschel et al 2003 *Cell* <a href="https://doi.org/10.1016/s0092-8674(03)00191-0">https://doi.org/10.1016/s0092-8674(03)00191-0</a> Grebien et al 2011 *Cell* <a href="https://doi.org/10.1016/j.cell.2011.08.046">https://doi.org/10.1016/j.cell.2011.08.046</a> Bigenzahn et al 2018 *Science* <a href="https://doi.org/10.1126/science.aap8210">https://doi.org/10.1126/science.aap8210</a> Heinz et al 2020 *Nature* <a href="https://doi.org/10.1038/s41586-020-2282-0">https://doi.org/10.1038/s41586-020-2282-0</a>

#### The mechanism of action of cancer drugs:

Developed "omics" approaches to elucidate the actual molecular impact of cancer drugs, in particular chemical proteomics approaches and integrated systems analysis. Identified new use for existing drugs and established principles to study drug synergy and drug transport. Currently we are working on new transporter drugs and proteostatic RAS regulators. 2000-present Cellzome, CeMM / ERC Adv grant Game of Gates /FWF grants. Co-invented and developed Functional Precision Medicine platform based on high content imagine and machine learning that was successful in first historical trial with patients.

Winter et al 2012 Nature Chemical Biology https://doi.org/10.1038/nchembio.1085
Winter et al 2014 Nature Chemical Biology https://doi.org/10.1038/nchembio.1590
Huber et al 2014 Nature https://doi.org/10.1038/nature13194
Rebsamen et al 2015 Nature https://doi.org/10.1038/nature14107
Vladimer et al 2017 Nat Chem Bio https://pubmed.ncbi.nlm.nih.gov/28437395/
Snijder et al 2017 Lancet Hematol https://pubmed.ncbi.nlm.nih.gov/29153976/
Girardi et al. 2020 Nature Chemical Biology https://doi.org/10.1038/s41589-020-0483-3
Kornauth et al. 2022 Cancer Discov. https://pubmed.ncbi.nlm.nih.gov/34635570/

# Systems biology and molecular networks:

A key project concerned the first genome-wide screens for protein complexes in eukaryotes, essentially creating a first-pass functional map of the cellular machinery of an eukaryotic cell- to this day one of the most highly cited papers on systems biology. Another milestone was the first physical and functional map of an entire human signaling pathway (combined interaction proteomics and RNA interference screen, TNF). Other important projects have been the systematic mapping of the proteomic impact of viral immuno-modulating genes. More recently, we identified the first "circular" metabolic network, formed by the co-regulatory patterns of cellular lipids as they are affected in inflammation. Currently we are creating a synthetic lethal genetic interaction map of cellular transporters, aiming at shedding light on the function of hundreds of poorly characterized cellular transporters. 2000-present Cellzome, CeMM/ IMI Grant ReSOLUTE (€ 24 M coordinator, € 8 M) and RESOLUTION (€ 2 M /€ 1 M), FWF Grants.

Gavin et al 2002 *Nature* <a href="https://doi.org/10.1038/415141a">https://doi.org/10.1038/415141a</a>
Gavin et al 2006 *Nature* <a href="https://doi.org/10.1038/04532">https://doi.org/10.1038/04532</a>
Pichlmair et al 2012 *Nature* <a href="https://doi.org/10.1038/nature11289">https://doi.org/10.1038/nature11289</a>
Koeberlin et al 2015 *Cell* <a href="https://doi.org/10.1016/j.cell.2015.05.051">https://doi.org/10.1016/j.cell.2015.05.051</a>
Girardi et al. 2020 *Nature Communications* <a href="https://doi.org/10.1038/s41467-020-19871-x">https://doi.org/10.1038/s41467-020-19871-x</a>

# Nutrient access in cancer, aging and neurodegeneration:

Through our work on membrane transporters we learned how to modulate nutrient access. Loss of cell identity in disease may be partly corrected by restoring /enforcing metabolic and epigenetic plasticity through differential regulation of transporter action. We started mapping nutrient requirements in cancer, aging and neurodegenerative diseases using iPSCs and organoids.

Li et al 2021 *Nature Metabolism* <a href="https://pubmed.ncbi.nlm.nih.gov/33972798/">https://pubmed.ncbi.nlm.nih.gov/33972798/</a>
Pemovska et al 2021 *Nature Communications* <a href="https://pubmed.ncbi.nlm.nih.gov/34907165/">https://pubmed.ncbi.nlm.nih.gov/34907165/</a>
Rebsamen et al 2022 *Life Sci Alliance* <a href="https://pubmed.ncbi.nlm.nih.gov/36114003/">https://pubmed.ncbi.nlm.nih.gov/37516113/</a>
Dvorak et al. 2023 *Cell Chem Bio* <a href="https://pubmed.ncbi.nlm.nih.gov/37516113/">https://pubmed.ncbi.nlm.nih.gov/37516113/</a>

# List of the ten most relevant publications: Giulio Superti-Furga

# equal contributions, \*correspondence when not last or co-correspondence

- 1. TASL is the SLC15A4-associated adaptor for IRF5 activation by TLR7-9. Heinz LX, Lee J, Kapoor U, Kartnig F, Sedlyarov V, Papakostas K, César-Razquin A, Essletzbichler P, Goldmann U, Stefanovic A, Bigenzahn JW, Scorzoni S, Pizzagalli MD, Bensimon A, Müller AC, King FJ, Li J, Girardi E, Mbow ML, Whitehurst CE, Rebsamen M\*, Superti-Furga G\*. *Nature*. 2020 May 13;581(7808):316-322.
- 2. LZTR1 is a regulator of RAS ubiquitination and signaling. Bigenzahn JW, Collu GM, Kartnig F, Pieraks M, Vladimer GI, Heinz LX, Sedlyarov V, Schischlik F, Fauster A, Rebsamen M, Parapatics K, Blomen VA, Müller AC, Winter GE, Kralovics R, Brummelkamp TR, Mlodzik M, Superti-Furga G. *Science*. 2018 Dec 7;362(6419):1171-1177.
- 3. SLC38A9 is a component of the lysosomal amino acid sensing machinery that controls mTORC1. Rebsamen M, Pochini L, Stasyk T, de Araújo ME, Galluccio M, Kandasamy RK, Snijder B, Fauster A, Rudashevskaya EL, Bruckner M, Scorzoni S, Filipek PA, Huber KV, Bigenzahn JW, Heinz LX, Kraft C, Bennett KL, Indiveri C, Huber LA, Superti-Furga G. *Nature*. 2015 Mar 26;519(7544):477-81.
- 4. Conserved Circular Network of Coregulated Lipids Modulates Innate Immune Responses. Köberlin MS, Snijder B, Heinz LX, Baumann CL, Fauster A, Vladimer GI, Gavin AC, Superti-Furga G. *Cell*. 2015 Jul 2;162(1):170-83.
- 5. Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. Huber KV, Salah E, Radic B, Gridling M, Elkins JM, Stukalov A, Jemth AS, Göktürk C, Sanjiv K, Strömberg K, Pham T, Berglund UW, Colinge J, Bennett KL, Loizou JI, Helleday T, Knapp S, Superti-Furga G. *Nature*. 2014 Apr 10;508(7495):222-7.
- 6. Viral immune modulators perturb the human molecular network by common and unique strategies. Pichlmair A, Kandasamy K, Alvisi G, Mulhern O, Sacco R, Habjan M, Binder M, Stefanovic A, Eberle CA, Goncalves A, Bürckstümmer T, Müller AC, Fauster A, Holze C, Lindsten K, Goodbourn S, Kochs G, Weber F, Bartenschlager R, Bowie AG, Bennett KL, Colinge J, Superti-Furga G. *Nature*. 2012 Jul 26;487(7408):486-90.
- 7. Targeting the SH2-kinase interface in Bcr-Abl inhibits leukemogenesis. Grebien F, Hantschel O\*, Wojcik J, Kaupe I, Kovacic B, Wyrzucki AM, Gish GD, Cerny-Reiter S, Koide A, Beug H, Pawson T, Valent P, Koide S, Superti-Furga G\*. *Cell* 2011 Oct 14:147(2):306-19.
- 8. Proteome survey reveals modularity of the yeast cell machinery. Gavin AC, Aloy, P, Grandi P, Krause R, Boesche M, Marzioch M, Rau C, Jensen LJ, Bastuck S, Dümplefled B, Edelmann A, Heurtier MA, Hoffmann V, Hoefert C, Michon M, Schirle M, Remor M, Bauer A, Bouwmeester T, Casari G, Drewes, G, Neubauer G, Rick JM, Kuster B, Bork P, Russell RB\*, and Superti-Furga G\*. *Nature* 2006 440(7084):631-6.
- 9. A myristate/phosphotyrosine switch regulates c-Abl. Hantschel O, Nagar B, Guettler S, Kretzschmar J, Dorey K, Kuriyan J\*, Superti-Furga G\*. *Cell* 2003 112, 845-857.
- 10. Functional organization of a eukaryotic proteome: systematic analysis of multi-protein complexes in Saccharomyces cerevisiae. Gavin AC, Bosche M, Krause R, Grandi P, Marzioch M, Bauer A, Schultz J, Rick JM, Michon AM, Cruciat CM, Remor M, Hofert C, Schelder M, Brajenovic M, Ruffner H, Merino A, Klein K, Hudak M, Dickson D, Rudi T, Gnau V, Bauch A, Bastuck S, Huhse B, Leutwein C, Heurtier MA, Copley RR, Edelmann A, Querfurth E, Rybin V, Drewes G, Raida M, Bouwmeester T, Bork P, Seraphin B, Kuster B, Neubauer G, Superti-Furga G. *Nature* 2002 415, 141-147.