Curriculum vitae

Giannino Del Sal
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Education and training

1988-1989	Research fellow in Molecular Oncogenesis, Cell and Genome Studies Unit, International Centre for Genetics and Biotechnology (ICGEB), Trieste, Italy.
1987	Research fellow in Molecular Oncogenesis, Cell and Differentiation Program, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany.
1985-1986	Research fellow in Biochemistry, Dipartimento di Biochimica, Università degli Studi di Trieste, Trieste, Italy.
23/11/1984	Laurea *summa cum laude* in Biology, Università degli Studi di Trieste, Trieste, Italy.

Positions and Employment

2012-2018	Director, Dipartimento di Scienze della Vita, Università degli Studi di Trieste, Trieste, Italy.
2001-present	Full Professor in Applied Biology, Università degli Studi di Trieste, Trieste, Italy.
1996-present	Head, Molecular Oncology Unit, LNCIB, Trieste, Italy.
1998-2001	Associate Professor in Applied Biology, Università degli Studi di Trieste, Trieste, Italy.
1991-1998	Assistant Professor in Applied Biology, Università degli Studi di Trieste, Trieste, Italy.
1994-1996	Visiting scientist, Laboratory of Cell Biology, Mitotix Inc., Cambridge, USA.
1992-1994	Researcher, LNCIB, Trieste, Italy.
1990-1991	Associate expert, Cell and Genome Studies Unit, International Centre for Genetics and Biotechnology (ICGEB), Trieste, Italy.

Editorial activity

2017-present	Member, Editorial Board of *Cell Death and Differentiation*
2017-present	Member, Editorial Board of *Journal of Molecular Cell Biology (JMCB).*
2008-present	Member, Advisory Editorial Board, *EMBO reports*.
2008-2011	Member, Advisory Editorial Board, *EMBO journal*.

Other experience and professional membership

2018-	Member, Scientific Standing Committee for the Pezcoller Symposia-Fondazione Pezcoller
2014-present	Member, Faculty, Joint PhD Program in Molecular Biology (JuMBO) of Scuola Internazionale Superiore di Studi Avanzati (SISSA), International Centre for Genetics and Biotechnology (ICGEB), Università degli Studi di Udine, Università degli Studi di Trieste.
2010-present	Member, Fellowship Scientific Committee, Associazione Italiana per la Ricerca sul Cancro (AIRC).
2006-2015	Member, International Scientific Advisory Board, Istituto Toscano Tumori (ITT).
2011-2012	Member, GEV panel of expert evaluators for Areas 5 and 6 (Gruppi di Esperti della Valutazione per l'Area Scienze Biologiche e per l'Area Scienze Mediche), National Agency for the Evaluation of Universities and Research Institutes (ANVUR).
2010-2012	Member, Research Evaluation Committee (CVR), Università degli Studi di Trieste.

2007-2012	Director, PhD School in Molecular Biomedicine, Università degli Studi di Trieste.
2004-2009	Member, Scientific Committee, Associazione Italiana per la Ricerca sul Cancro (AIRC).
2004-2007	Member, Scientific Committee, Consorzio di Biomedicina Molecolare (CBM), Trieste, Italy.
Over 15 years experience	Reviewer for national and international funding organizations, among which: European Commission, Israeli Science Foundation, Cancer Research (UK), Wellcome Trust (UK), Research Council of Hong Kong, World Wide Association for Cancer Research (UK), Fondation contre le Cancer (Be), EMBO (Germany), Associazione Italiana per la Ricerca sul Cancro (AIRC, Italy) and many others.
Over 15 years experience	Reviewer for *Nature*, *Nature Medicine, Nature Cell Biology*, *Molecular Cell*, *Science*, *EMBO Journal*, *EMBO Reports*, *Journal of Cell Biology*, *Proceedings of the National Academy of Sciences USA*, *Cancer Research*, *Oncogene*, *Cell Death and Differentiation*, *Journal of Cell Science* and many others.

Honors and Awards

2006	Membership in recognition of his scientific achievements, European Molecular Biology Organization (EMBO).

Scientific Profile

Since the beginning of his scientific career, Del Sal has devoted himself to the study of cancer biology, integrating different aspects, approaches and technologies and providing seminal contributions to the elucidation of key mechanisms in the pathogenesis of tumours. His work integrates the study of the mechanisms of tumour suppression in health and cancer, the investigation of the role of different oncogenic pathways in cancer development and metastasis, as well as more translational research devoted to the development of novel strategies and tools for cancer therapy.

Among the most significant scientific discoveries:

- the first cloning and characterization in the context of growth arrest of GAS1, a Sonic Hedgehog binding protein (Del Sal et al., *Cell* 1992; Del Sal et al., *Proc Natl Acad Sci USA* 1994);

as principal investigator:

- the discovery of new post-translational modifications (Gostissa et al., *EMBO J* 1999) and new sub-cellular localization of the tumor suppressor p53 (Fogal et al., *EMBO J* 2000);
- the discovery of new regulatory mechanisms of wt p53 and p53 family proteins (Zacchi et al., *Nature* 2002; Mantovani et al., *Mol Cell* 2004; Mantovani et al., *Nat Struct Mol Biol* 2007; Drost et al., *Nat Cell Biol* 2010);
- the discovery of the proteasome machinery as a key target of a common gain-of-function program shared by diverse missense mutants of p53 in cancer (Walerych et al., *Nat Cell Biol* 2016).
- the discovery of the impact of the prolyl-isomerase Pin1 on Notch pathway in proliferation and maintenance of normal and cancer stem cells of the breast, as well as on the full activation of mutant p53 oncogenic functions and the identification and characterization of the first covalent Pin1 inhibitor selectively targeting cancer cells by a dual mechanism of action. (Rustighi et al., *Nat Cell Biol* 2009; Rustighi et al., *EMBO Mol Med* 2014; Girardini et al., *Cancer Cell* 2011; Campaner et al *Nat Commun* 2017);
- the discovery of the metabolic control of the Hippo pathway transducers YAP/TAZ by the mevalonate pathway (Sorrentino et al., *Nat Cell Biol* 2014), and the discovery that mevalonate and mechanical cues regulate the stability and function of mutant p53 (Ingallina et al *Nat Cell Biol* 2018). These results 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).
- the discovery of the hormonal control by Glucocorticoids on the Yap activity in breast cancer (Sorrentino et al *Nat Commun* 2017).

Patents

- Patent US8822420 B2 - Peptides and aptamers therof as specific modulators of mutant p53 function.
- Patent WO2012172511 A1: Method for the prognosis of breast cancer based on the expression of the gene PIN1 in combination with mutations in the gene TP53.

Scientific Publications

More than130 among peer-reviewed research articles, reviews and book chapters.

A selection of recent relevant publication (2013-2018):

1. Caroli J, Sorrentino G, Forcato M, **Del Sal G**, Bicciato S. (2018) GDA, a web-based tool for Genomics and Drugs integrated analysis. ***Nucleic Acids Res***.46(W1): W148-W156.doi: 10.1093/nar/gky434.
2. Ingallina E, Sorrentino G, Bertolio R, Lisek K, Zannini A, Azzolin L, Severino LU, Scaini D, Mano M, Mantovani F, Rosato A, Bicciato S, Piccolo S, **Del Sal G**. (2018) Mechanical cues control mutant p53 stability through a mevalonate-RhoA axis. ***Nat Cell Biol***. 20(1):28-35. doi: 10.1038/s41556-017-0009-8.
3. Liao P, Zeng SX, Zhou X, Chen T, Zhou F, Cao B, Jung JH, **Del Sal G**, Luo S, Lu H. (2017) Mutant p53 Gains Its Function via c-Myc Activation upon CDK4 Phosphorylation at Serine 249 and Consequent PIN1 Binding. ***Mol Cell***. 68(6):1134-1146.e6. doi: 10.1016/j.molcel.2017.11.006.
4. Tan MH, Li Q, Shanmugam R, Piskol R, Kohler J, Young AN, Liu KI, Zhang R, Ramaswami G, Ariyoshi K, Gupte A, Keegan LP, George CX, Ramu A, Huang N, Pollina EA, Leeman DS, Rustighi A, Goh YPS; GTEx Consortium; Laboratory, Data Analysis &Coordinating Center (LDACC)—Analysis Working Group; Statistical Methods groups—Analysis Working Group; Enhancing GTEx (eGTEx) groups; NIH Common Fund; NIH/NCI; NIH/NHGRI; NIH/NIMH; NIH/NIDA; Biospecimen Collection Source Site—NDRI; Biospecimen Collection Source Site—RPCI; Biospecimen Core Resource—VARI; Brain Bank Repository—University of Miami Brain Endowment Bank; Leidos Biomedical—Project Management; ELSI Study; Genome Browser Data Integration &Visualization—EBI; Genome Browser Data Integration &Visualization—UCSC Genomics Institute, University of California Santa Cruz, Chawla A, **Del Sal G**, Peltz G, Brunet A, Conrad DF, Samuel CE, O'Connell MA, Walkley CR, Nishikura K, Li JB. (2017) Dynamic landscape and regulation of RNA editing in mammals. ***Nature***. 550(7675):249-254. doi: 10.1038/nature24041.
5. Campaner E, Rustighi A, Zannini A, Cristiani A, Piazza S, Ciani Y, Kalid O, Golan G, Baloglu E, Shacham S, Valsasina B, Cucchi U, Pippione AC, Lolli ML, Giabbai B, Storici P, Carloni P, Rossetti G, Benvenuti F, Bello E, D'Incalci M, Cappuzzello E, Rosato A, **Del Sal G**. (2017) A covalent PIN1 inhibitor selectively targets cancer cells by a dual mechanism of action. ***Nat Commun***. 8:15772. doi: 10.1038/ncomms15772.
6. Sorrentino G, Ruggeri N, Zannini A, Ingallina E, Bertolio R, Marotta C, Neri C, Cappuzzello E, Forcato M, Rosato A, Mano M, Bicciato S, **Del Sal G**. (2017) Glucocorticoid receptor signalling activates YAP in breast cancer. ***Nat Commun***. 8:14073. doi: 10.1038/ncomms14073.
7. Walerych D, Lisek K, Sommaggio R, Piazza S, Ciani Y, Dalla E, Rajkowska K, Gaweda-Walerych K, Ingallina E, Tonelli C, Morelli MJ, Amato A, Eterno V, Zambelli A, Rosato A, Amati B, Wiśniewski JR, **Del Sal G**. (2016). Proteasome machinery is instrumental in a common gain-of-function program of the p53 missense mutants in cancer. ***Nat Cell Biol*** 18(8):897-909. doi: 10.1038/ncb3380. PMID: 27347849. IF 19,679.
8. Vermezovic J, Adamowicz M, Santarpia L, Rustighi A, Forcato M, Lucano C, Massimiliano L, Costanzo V, Bicciato S, **Del Sal G**, d'Adda di Fagagna F. (2015). Notch is a direct negative regulator of the DNA-damage response. ***Nat Struct Mol Biol*** 22(5):417-24. doi: 10.1038/nsmb.3013. PMID: 25895060.
9. Giorgi C, Bonora M, Sorrentino G, Missiroli S, Poletti F, Suski JM, Galindo Ramirez F, Rizzuto R, Di Virgilio F, Zito E, Pandolfi PP, Wieckowski MR, Mammano F, **Del Sal G**, Pinton P. (2015). p53 at the endoplasmic reticulum regulates apoptosis in a Ca2+-dependent manner. ***Proc Natl Acad Sci USA*** 112(6):1779-84. doi: 10.1073/pnas.1410723112. PMID: 25624484.
10. Sorrentino G, Ruggeri N, Specchia V, Cordenonsi M, Mano M, Dupont S, Manfrin A, Ingallina E, Sommaggio R, Piazza S, Rosato A, Piccolo S, **Del Sal G**. (2014). Metabolic control of YAP and TAZ by the mevalonate pathway. ***Nat Cell Biol*** 16(4):357-66. doi: 10.1038/ncb2936. PMID: 24658687.

11. Rustighi A, Zannini A, Tiberi L, Sommaggio R, Piazza S, Sorrentino G, Nuzzo S, Tuscano A, Eterno V, Benvenuti F, Santarpia L, Aifantis I, Rosato A, Bicciato S, Zambelli A, **Del Sal G**. (2014). Prolyl-isomerase Pin1 controls normal and cancer stem cells of the breast. ***EMBO Mol Med*** 6(1):99-119. doi: 10.1002/emmm.201302909. PMID: 24357640.
12. Bitomsky N, Conrad E, Moritz C, Polonio-Vallon T, Sombroek D, Schultheiss K, Glas C, Greiner V, Herbel C, Mantovani F, **Del Sal G**, Peri F, Hofmann TG. (2013). Autophosphorylation and Pin1 binding coordinate DNA damage-induced HIPK2 activation and cell death. ***Proc Natl Acad Sci USA*** 110(45):E4203-12. doi: 10.1073/pnas.1310001110. PMID: 24145406.
13. Steger M, Murina O, Hühn D, Ferretti LP, Walser R, Hänggi K, Lafranchi L, Neugebauer C, Paliwal S, Janscak P, Gerrits B, **Del Sal G**, Zerbe O, Sartori AA. (2013). Prolyl isomerase PIN1 regulates DNA double-strand break repair by counteracting DNA end resection. ***Mol Cell*** 50(3):333-43. doi: 10.1016/j.molcel.2013.03.023. PMID: 23623683.
14. Sonego M, Schiappacassi M, Lovisa S, Dall'Acqua A, Bagnoli M, Lovat F, Libra M, D'Andrea S, Canzonieri V, Militello L, Napoli M, Giorda G, Pivetta B, Mezzanzanica D, Barbareschi M, Valeri B, Canevari S, Colombatti A, Belletti B, **Del Sal G**, Baldassarre G. (2013). Stathmin regulates mutant p53 stability and transcriptional activity in ovarian cancer. ***EMBO Mol Med*** 5(5):707-22. doi: 10.1002/emmm.201201504. PMID: 23610071.
15. Sorrentino G, Mioni M, Giorgi C, Ruggeri N, Pinton P, Moll U, Mantovani F, **Del Sal G**. (2013). The prolyl-isomerase Pin1 activates the mitochondrial death program of p53. ***Cell Death Differ*** 0(2):198-208. doi: 10.1038/cdd.2012.112. PMID: 22935610.

A selection of relevant publications from previous years:

1. Grison A, Mantovani F, Comel A, Agostoni E, Gustincich S, Persichetti F, **Del Sal G**. (2011). Ser46 phosphorylation and prolyl-isomerase Pin1-mediated isomerization of p53 are key events in p53-dependent apoptosis induced by mutant huntingtin. ***Proc Natl Acad Sci USA*** 108(44):17979-84. doi: 10.1073/pnas.1106198108. PMID: 22011578.
2. Girardini JE, Napoli M, Piazza S, Rustighi A, Marotta C, Radaelli E, Capaci V, Jordan L, Quinlan P, Thompson A, Mano M, Rosato A, Crook T, Scanziani E, Means AR, Lozano G, Schneider C, **Del Sal G**. (2011). A Pin1/mutant p53 axis promotes aggressiveness in breast cancer. ***Cancer Cell*** 20(1):79-91. doi: 10.1016/j.ccr.2011.06.004. PMID: 21741598.
3. Collavin L, Lunardi A, **Del Sal G**. (2010). p53-family proteins and their regulators: hubs and spokes in tumor suppression. ***Cell Death Differ*** 17(6):901-11. doi: 10.1038/cdd.2010.35. Review. PMID: 20379196.
4. Lunardi A, Di Minin G, Provero P, Dal Ferro M, Carotti M, **Del Sal G**, Collavin L. (2010). A genome-scale protein interaction profile of Drosophila p53 uncovers additional nodes of the human p53 network. ***Proc Natl Acad Sci USA*** 107(14):6322-7. doi: 10.1073/pnas.1002447107. PMID: 20308539.
5. Drost J, Mantovani F, Tocco F, Elkon R, Comel A, Holstege H, Kerkhoven R, Jonkers J, Voorhoeve PM, Agami R, **Del Sal G**. (2010). BRD7 is a candidate tumour suppressor gene required for p53 function. ***Nat Cell Biol*** 12(4):380-9. doi: 10.1038/ncb2038. PMID: 20228809.
6. Manganaro L, Lusic M, Gutierrez MI, Cereseto A, **Del Sal G**, Giacca M. (2010). Concerted action of cellular JNK and Pin1 restricts HIV-1 genome integration to activated CD4+ T lymphocytes. ***Nat Med*** 16(3):329-33. doi: 10.1038/nm.2102. PMID: 20173753.
7. Gianni' M, Boldetti A, Guarnaccia V, Rambaldi A, Parrella E, Raska I Jr, Rochette-Egly C, **Del Sal G**, Rustighi A, Terao M, Garattini E. (2009). Inhibition of the peptidyl-prolyl-isomerase Pin1 enhances the responses of acute myeloid leukemia cells to retinoic acid via stabilization of RARalpha and PML-RARalpha. ***Cancer Res*** 69(3):1016-26. doi: 10.1158/0008-5472.CAN-08-2603. PMID: 19155306.
8. Rustighi A, Tiberi L, Soldano A, Napoli M, Nuciforo P, Rosato A, Kaplan F, Capobianco A, Pece S, Di Fiore PP, **Del Sal G**. (2009). The prolyl-isomerase Pin1 is a Notch1 target that enhances Notch1 activation in cancer. ***Nat Cell Biol*** 11(2):133-42. doi: 10.1038/ncb1822. PMID: 19151708.
9. Guida E, Bisso A, Fenollar-Ferrer C, Napoli M, Anselmi C, Girardini JE, Carloni P, **Del Sal G**. (2008). Peptide aptamers targeting mutant p53 induce apoptosis in tumor cells. ***Cancer Res*** 68(16):6550-8. doi: 10.1158/0008-5472.CAN-08-0137. PMID: 18701478.

10. Mantovani F, Tocco F, Girardini J, Smith P, Gasco M, Lu X, Crook T, **Del Sal G**. (2007). The prolyl isomerase Pin1 orchestrates p53 acetylation and dissociation from the apoptosis inhibitor iASPP. ***Nat Struct Mol Biol*** 14(10):912-20. PMID: 17906639.
11. Zita MM, Marchionni I, Bottos E, Righi M, **Del Sal G**, Cherubini E, Zacchi P. (2007). Post-phosphorylation prolyl isomerisation of gephyrin represents a mechanism to modulate glycine receptors function. ***EMBO J*** 26(7):1761-71. PMID: 17347650.
12. Pinton P, Rimessi A, Marchi S, Orsini F, Migliaccio E, Giorgio M, Contursi C, Minucci S, Mantovani F, Wieckowski MR, **Del Sal G**, Pelicci PG, Rizzuto R. (2007). Protein kinase C beta and prolyl isomerase 1 regulate mitochondrial effects of the life-span determinant p66Shc. ***Science*** 315(5812):659-63. PMID: 17272725.
13. Bergamaschi D, Samuels Y, Sullivan A, Zvelebil M, Breyssens H, Bisso A, **Del Sal G**, Syed N, Smith P, Gasco M, Crook T, Lu X. (2006). iASPP preferentially binds p53 proline-rich region and modulates apoptotic function of codon 72-polymorphic p53. ***Nat Genet*** 38(10):1133-41. PMID: 16964264.
14. Gresko E, Roscic A, Ritterhoff S, Vichalkovski A, **Del Sal G**, Schmitz ML. (2006). Autoregulatory control of the p53 response by caspase-mediated processing of HIPK2. ***EMBO J*** 25(9):1883-94. PMID: 16601678.
15. Berger M, Stahl N, **Del Sal G**, Haupt Y. (2005). Mutations in proline 82 of p53 impair its activation by Pin1 and Chk2 in response to DNA damage. ***Mol Cell Biol*** 25(13):5380-8. PMID: 15964795.
16. Strano S, Monti O, Pediconi N, Baccarini A, Fontemaggi G, Lapi E, Mantovani F, Damalas A, Citro G, Sacchi A, **Del Sal G**, Levrero M, Blandino G. (2005). The transcriptional coactivator Yes-associated protein drives p73 gene-target specificity in response to DNA Damage. ***Mol Cell*** 18(4):447-59. PMID: 15893728.
17. Gostissa M, Morelli M, Mantovani F, Guida E, Piazza S, Collavin L, Brancolini C, Schneider C, **Del Sal G**. (2004). The transcriptional repressor hDaxx potentiates p53-dependent apoptosis. ***J Biol Chem*** 279(46):48013-23. PMID: 15339933.
18. Mantovani F, Piazza S, Gostissa M, Strano S, Zacchi P, Mantovani R, Blandino G, **Del Sal G**. (2004). Pin1 links the activities of c-Abl and p300 in regulating p73 function. ***Mol Cell*** 14(5):625-36. PMID: 15175157.
19. Collavin L, Gostissa M, Avolio F, Secco P, Ronchi A, Santoro C, **Del Sal G**. (2004). Modification of the erythroid transcription factor GATA-1 by SUMO-1. ***Proc Natl Acad Sci USA*** 101(24):8870-5. PMID: 15173587.
20. Zacchi P, Gostissa M, Uchida T, Salvagno C, Avolio F, Volinia S, Ronai Z, Blandino G, Schneider C, **Del Sal G**. (2002). The prolyl isomerase Pin1 reveals a mechanism to control p53 functions after genotoxic insults. ***Nature*** 419(6909):853-7. PMID: 12397362.
21. D'Orazi G, Cecchinelli B, Bruno T, Manni I, Higashimoto Y, Saito S, Gostissa M, Coen S, Marchetti A, **Del Sal G**, Piaggio G, Fanciulli M, Appella E, Soddu S. (2002). Homeodomain-interacting protein kinase-2 phosphorylates p53 at Ser 46 and mediates apoptosis. ***Nat Cell Biol*** 4(1):11-9. PMID: 11780126.
22. Benetti R, **Del Sal G**, Monte M, Paroni G, Brancolini C, Schneider C. (2001). The death substrate Gas2 binds m-calpain and increases susceptibility to p53-dependent apoptosis. ***EMBO J*** 20(11):2702-14. PMID: 11387205.
23. Fogal V, Gostissa M, Sandy P, Zacchi P, Sternsdorf T, Jensen K, Pandolfi PP, Will H, Schneider C, **Del Sal G**. (2000). Regulation of p53 activity in nuclear bodies by a specific PML isoform. ***EMBO J*** 19(22):6185-95. PMID: 11080164.
24. Sandy P, Gostissa M, Fogal V, Cecco LD, Szalay K, Rooney RJ, Schneider C, **Del Sal G**. (2000). p53 is involved in the p120E4F-mediated growth arrest. ***Oncogene*** 19(2):188-99. PMID: 10644996.
25. Gostissa M, Hengstermann A, Fogal V, Sandy P, Schwarz SE, Scheffner M, **Del Sal G**. (1999). Activation of p53 by conjugation to the ubiquitin-like protein SUMO-1. ***EMBO J*** 18(22):6462-71. PMID: 10562558.
26. **Del Sal G**, Murphy M, Ruaro E, Lazarevic D, Levine AJ, Schneider C. (1996). Cyclin D1 and p21/waf1 are both involved in p53 growth suppression. ***Oncogene*** 12(1):177-85. PMID: 8552389.
27. **Del Sal G**, Ruaro EM, Utrera R, Cole CN, Levine AJ, Schneider C. (1995). Gas1-induced growth suppression requires a transactivation-independent p53 function. ***Mol Cell Biol*** 15(12):7152-60. PMID: 8524283.

28. Pagano M, Tam SW, Theodoras AM, Beer-Romero P, **Del Sal G**, Chau V, Yew PR, Draetta GF, Rolfe M. (1995). Role of the ubiquitin-proteasome pathway in regulating abundance of the cyclin-dependent kinase inhibitor p27. ***Science*** 269(5224):682-5. PMID: 7624798.
29. **Del Sal G**, Collavin L, Ruaro ME, Edomi P, Saccone S, Valle GD, Schneider C. (1994). Structure, function, and chromosome mapping of the growth-suppressing human homologue of the murine gas1 gene. ***Proc Natl Acad Sci USA*** 91(5):1848-52. PMID: 8127893.
30. **Del Sal G**, Ruaro ME, Philipson L, Schneider C. (1992). The growth arrest-specific gene, gas1, is involved in growth suppression. ***Cell*** 70(4):595-607. PMID: 1505026.