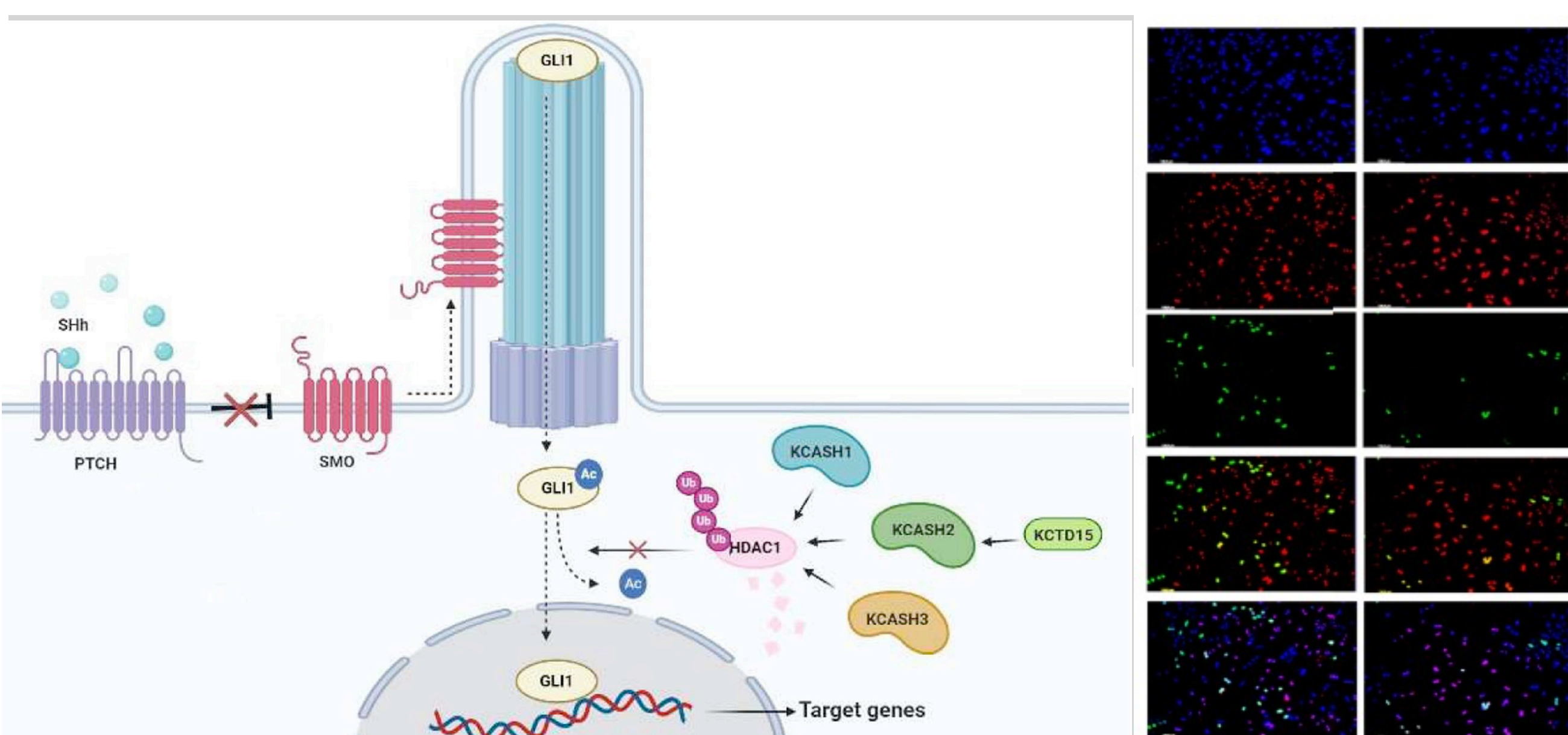


# Laboratory of Experimental Oncology and preclinical models



## General description of the activities

Use of *in vitro* cellular models and mouse models for understanding the molecular mechanisms of tumorigenesis and for the validation of potential therapeutic targets.

Role	Name	Position	E-mail	Publications	Keywords
Lab head	Prof. Enrico De Smaele	Full professor	<a href="mailto:Enrico.desmaele@uniroma1.it">Enrico.desmaele@uniroma1.it</a>	<a href="https://pubmed.ncbi.nlm.nih.gov/?term=de+smaele+e&amp;sort=date&amp;size=50">https://pubmed.ncbi.nlm.nih.gov/?term=de+smaele+e&amp;sort=date&amp;size=50</a>	Cancer, Medulloblastoma, Hh pathway, NF-kappaB, KCASH, KCTD1, KCTD21
Lab members	Prof. Marta Moretti	Tenure Track Researcher	<a href="mailto:Marta.moretti@uniroma1.it">Marta.moretti@uniroma1.it</a>	<a href="https://orcid.org/0000-0003-4705-6442">https://orcid.org/0000-0003-4705-6442</a>	DNA methylation, microRNAs, Hedgehog pathway, CRC
	Dr. Fabio Bordini	Post-doc	<a href="mailto:Fabio.bordini@uniroma1.it">Fabio.bordini@uniroma1.it</a>	<a href="https://pubmed.ncbi.nlm.nih.gov/?term=fabio+bordini&amp;sort=date&amp;size=50">https://pubmed.ncbi.nlm.nih.gov/?term=fabio+bordini&amp;sort=date&amp;size=50</a>	Ubiquitination, neural development, SMURF1 and SMURF2, Gli1
	Dr. Adriano Apostolico	PhD student	<a href="mailto:Adriano.apostolico@uniroma1.it">Adriano.apostolico@uniroma1.it</a>	<a href="https://pubmed.ncbi.nlm.nih.gov/?term=adriano+apostolico&amp;sort=date&amp;size=50">https://pubmed.ncbi.nlm.nih.gov/?term=adriano+apostolico&amp;sort=date&amp;size=50</a>	Neural development, hedgehog inhibitors
	Dr Faranak Taj Mir	PhD student	<a href="mailto:Faranak.tajmir@uniroma1.it">Faranak.tajmir@uniroma1.it</a>	<a href="https://www.scopus.com/authid/detail.uri?authorId=57214780465">https://www.scopus.com/authid/detail.uri?authorId=57214780465</a>	miRNAs, hedgehog pathway, KCASH2
	Dr Sara Bellardinelli	PhD student	<a href="mailto:Sara.bellardinelli@uniroma1.it">Sara.bellardinelli@uniroma1.it</a>	<a href="https://pubmed.ncbi.nlm.nih.gov/?term=bellardinelli+s&amp;sort=date&amp;size=50">https://pubmed.ncbi.nlm.nih.gov/?term=bellardinelli+s&amp;sort=date&amp;size=50</a>	Immune system, KCTD1, KCASH2, Hedgehog pathway
	Dr Gloria Terriaca	PhD student	<a href="mailto:Gloria.terriaca@uniroma1.it">Gloria.terriaca@uniroma1.it</a>	<a href="https://pubmed.ncbi.nlm.nih.gov/?term=terriaca+g&amp;sort=date&amp;size=50">https://pubmed.ncbi.nlm.nih.gov/?term=terriaca+g&amp;sort=date&amp;size=50</a>	CRC models, Hedgehog pathway, KCASH2

## Previous and current research

The main research activities can be subdivided in two major topics:

1) Study of the mechanisms which regulate the potentially oncogenic Hedgehog (Hh) pathway in cerebellum and in medulloblastoma, and search for potential therapeutical targets:

-Identification of KCTD11/KCASH1, KCTD21/KCASH2 and KCTD6/KCASH3.

-Identification of novel Hedgehog target genes (Nhh1 and Insm1), involved in cerebellar development and tumorigenesis;

-Analysis of miRNAs expression during cerebellar development and in medulloblastoma. Use of miRNAs expression profiling for classification of medulloblastoma subtypes; identification of miRNAs targeting the Hedgehog pathway;

- identification and characterization of miRNAs involved in Hedgehog modulation and in cancer cell stemness;

- Identification of miRNAs involved in modulation of KCASH2 expression;

- Identification of new KCASH2 interactors: KCTD15 and KCTD1 as positive modulators of KCASH2 protein stability;

Generation and characterization of the KCASH2 KO mouse model: the role of KCASH2 in cerebellar development, in mouse fertility and in tumorigenesis *in vivo*;

Study of the role of KCASH2 in the modulation of cell cycle and chromosomal instability/aneuploidy.

Study of KCASH2 promoter and analysis of its transcriptional modulators.

2) Study on the role played by the transcription factor NF-kB in cell survival and cancer:

- characterization of the novel antiapoptotic gene Gadd45β, regulated by NF-kB;

- development of therapeutic molecules able to target Gadd45β;

- role of ROS in the regulation of apoptosis by NF-kB, and identification of the gene FHC involved in this regulation;

- role of NF-kB in the control of energy homeostasis by regulation of mitochondrial respiration;

## Selected Publications

- Lospinoso Severini L, ... De Smaele E, et al., *Cell Death Differ.* 2024 Feb;31(2):170-187. doi: 10.1038/s41418-023-01246-6.
- Di Fiore A, Bellardinelli S, ... Moretti M, De Smaele E. *Neoplasia.* 2023 Sep;43:100926. doi: 10.1016/j.neo.2023.100926.
- Angrisani A, Di Fiore A, ... Moretti M, De Smaele E. *Front Cell Dev Biol.* 2021 Apr 8;9:638508. doi:10.3389/fcell.2021.638508.
- Akman M, Belisario DC, ... De Smaele E, Riganti C. *J Exp Clin Cancer Res.* 2021 Jan 11;40(1):28. doi: 10.1186/s13046-020-01824-3.
- Coni S, ... De Smaele E, et al., *Cell Death Dis.* 2020 Dec 10;11(12):1045. doi: 10.1038/s41419-020-03174-6.
- Piombi E, Angrisani A, ... De Smaele E. *Oncogenesis.* 2019 Nov 4;8(11):64. doi: 10.1038/s41389-019-0175-6.
- Bufalieri F, Infante P, ... De Smaele E, et al., *Nat Commun.* 2019 Jul 24;10(1):3304. doi: 10.1038/s41467-019-11093-0.
- Infante P, ... De Smaele E, et al., *Nat Commun.* 2018 Mar 7;9(1):976. doi: 10.1038/s41467-018-03339-0.
- D'Amico D, Antonucci L, ...L, De Smaele E, et al., *Dev Cell.* 2015 Oct 12;35(1):21-35. doi: 10.1016/j.devcel.2015.09.008.
- Mauro C, Leow SC, Anso E, Rocha S, Thotakura AK, Tornatore L, Moretti M, De Smaele E, et al., *Nature Cell Biol.* 2011; 13:1272-9.
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- Canettieri G, Di Marcotullio L, Greco A, Coni S, Antonucci L, Infante P, Pietrosanti L, De Smaele E, et al., *Nature Cell Biol.* 2010; 12:132-42.
- Ferretti E\*, De Smaele E\*, et al., *Int J Cancer.* 2009; 124:568-77. \*Equal contributors.
- Ferretti E\*, De Smaele E\*, et al., *EMBO J.* 2008; 27:2616-27. \*Equal contributors.
- De Smaele E et al., *Neoplasia.* 2008; 10:89-98.
- Di Marcotullio L, Ferretti E, Greco A, De Smaele E, et al., *Nature Cell Biology.* 2006; 8:1415-23.
- Pham C.G., Bubici C., Zazzeroni F., Papa S., Jones J., Alvarez K., Jayawardena S., De Smaele E., et al., *Cell.* 2004; 119:529-42.
- \*Di Marcotullio L., \*Ferretti E., \*De Smaele E., et al., *Proc Natl Acad Sci U S A.* 2004; 101:10833-8. \*equal contributors
- Papa S, Zazzeroni F, Bubici C, Jayawardena S, Alvarez K, Matsuda S, Nguyen DU, Pham CG, Nelsbach AH, Melis T, De Smaele E, et al., *Nature Cell Biology* 2004; 6:146-53.
- Zazzeroni F, Papa S, De Smaele E, et al., *Nature* 2003, 424:742.
- De Smaele E., et al., *Nature.* 2001; 414: 308-13.

## Most recent grants

- PI of the PRIN 2022 project: "Novel approaches for the characterization and modulation of the oncogenic Sonic Hedgehog pathway in colorectal cancer. Identification of new potential prognostic markers and therapeutic targets." budget: 210'489 €;

- Co-PI and Responsible of La Sapienza's research unit, PRIN 2022 PNRR project P2022LZXNW\_002, "Simultaneous inhibition of multiple signaling transduction pathways by drugs combination in poor prognosis tumors" budget 117'000 €;

- 2023-current. PI of the PNRR project PE6, "HEAL ITALIA", Spoke 2 Sapienza "Intelligent Health", (PI) budget 435'169,14 €;

- Years 12/2014 - 12/2015: scientific manager of the project "PON Ricerca e competitività PON01\_02464" (New Biotechnological Drugs Active Through The Modulation Of Receptor Activity); approved budget 4'963'000 €. Consorzio PitecnoBio, Catania;

