Molecular oncology

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RET is the functional receptor tyrosine kinase for growth factors of the GDNF family. Gain-of-function genetic lesions convert RET into a driver oncogene in several human malignancies, including papillary thyroid carcinoma, medullary thyroid carcinoma and lung adenocarcinoma. Our project aims at: i) elucidating the mechanisms through which various genetic lesions (gene fusions, InDels, single amino-acid substitutions) activate RET oncogenic potential; ii) characterize the activity of rationally-designed RET small molecule kinase inhibitors (TKIs); iii) characterize the molecular mechanisms mediating RET resistance to RET-targeted TKIs. These studies are run in collaboration with the group of Francesca Carlomagno at the DMMBM.

1. RET Gene Fusions in Malignancies of the Thyroid and Other Tissues.
Santoro M, Moccia M, Federico G, Carlomagno F.Genes (Basel). 2020 Apr 15;11(4):424. doi: 10.3390/genes11040424.PMID: 32326537

2. Bioisosteric Discovery of NPA101.3, a Second-Generation RET/VEGFR2 Inhibitor Optimized for Single-Agent Polypharmacology.
Moccia M, Frett B, Zhang L, Lakkaniga NR, Briggs DC, Chauhan R, Brescia A, Federico G, Yan W, Santoro M, McDonald NQ, Li HY, Carlomagno F.J Med Chem. 2020 May 14;63(9):4506-4516. doi: 10.1021/acs.jmedchem.9b01336. Epub 2020 Apr 28.PMID: 32298114

3. Insights into Current Tropomyosin Receptor Kinase (TRK) Inhibitors: Development and Clinical Application.
Yan W, Lakkaniga NR, Carlomagno F, Santoro M, McDonald NQ, Lv F, Gunaganti N, Frett B, Li HY.J Med Chem. 2019 Feb 28;62(4):1731-1760. doi: 10.1021/acs.jmedchem.8b01092. Epub 2018 Sep 19.PMID: 30188734

4. Association between DNA methylation profile and malignancy in follicular-patterned thyroid neoplasms.
Affinito O, Salerno P, D'Alessio A, Cuomo M, Florio E, Carlomagno F, Proietti A, Giannini R, Basolo F, Chiariotti L, Cocozza S, Santoro M.Endocr Relat Cancer. 2019 Apr 1;26(4):451-462. doi: 10.1530/ERC-18-0308. Epub 2019 Feb 1.PMID: 30753136

5. Oncogene-induced senescence and its evasion in a mouse model of thyroid neoplasia.
Bellelli R, Vitagliano D, Federico G, Marotta P, Tamburrino A, Salerno P, Paciello O, Papparella S, Knauf JA, Fagin JA, Refetoff S, Troncone G, Santoro M.Mol Cell Endocrinol. 2018 Jan 15;460:24-35. doi: 10.1016/j.mce.2017.06.023. Epub 2017 Jun 23.PMID: 28652169