



The biology of malignant peripheral nerve sheath tumours

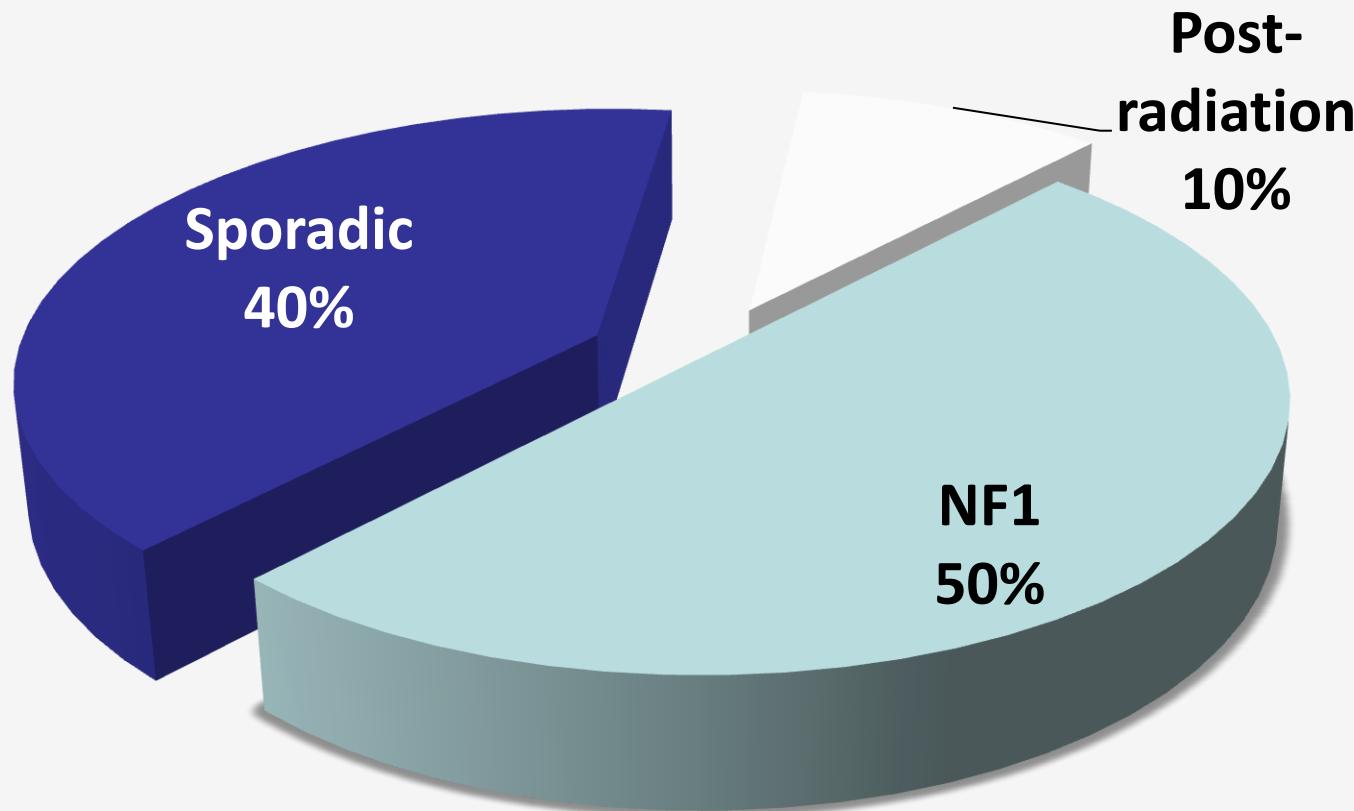
Enrique de Alava

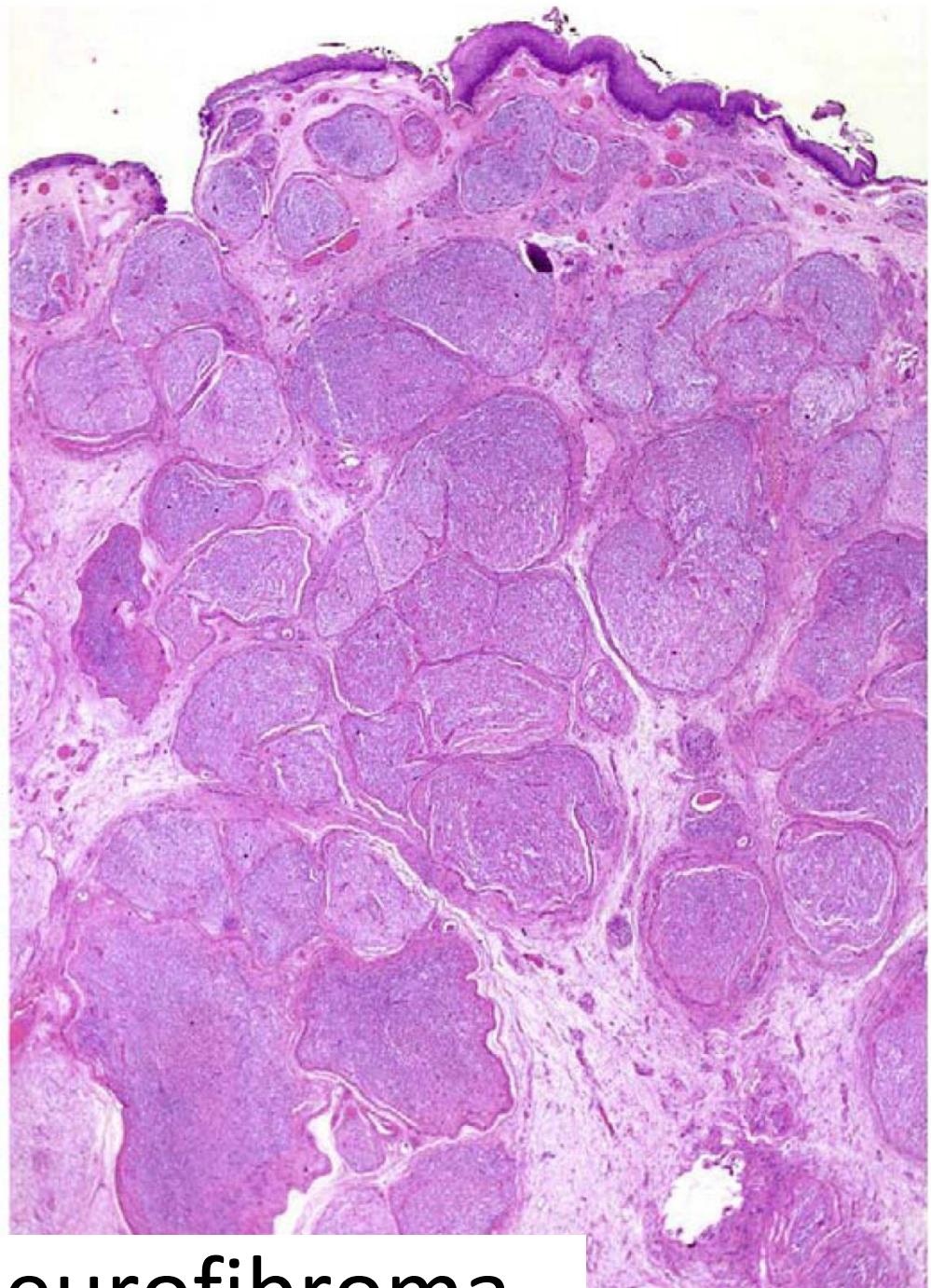


Disclosure slide

- Research support:
Pfizer, PharmaMar, Celgene, AstraZeneca
- Honoraria: Roche, Glaxo

Three clinical settings





Plexiform Neurofibroma

Neurofibromatosis type 1.
Neurofibromin 1
NF1

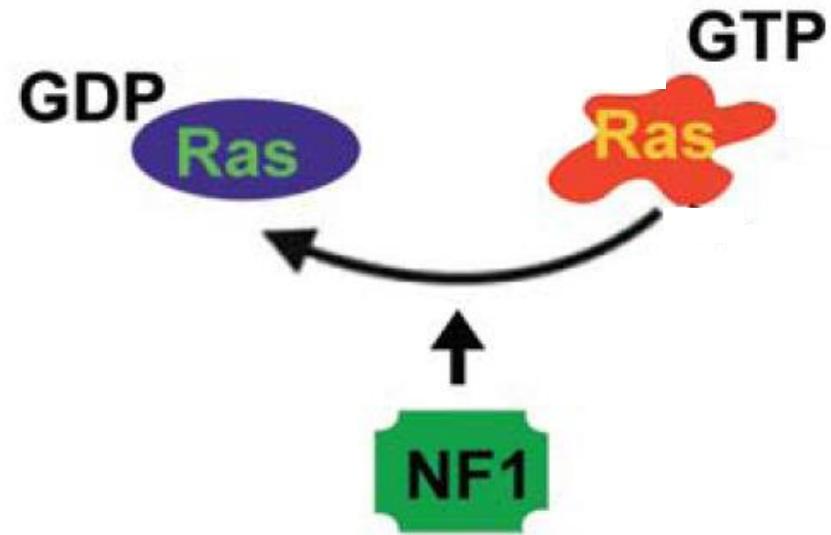
Neurofibromatosis type 1.

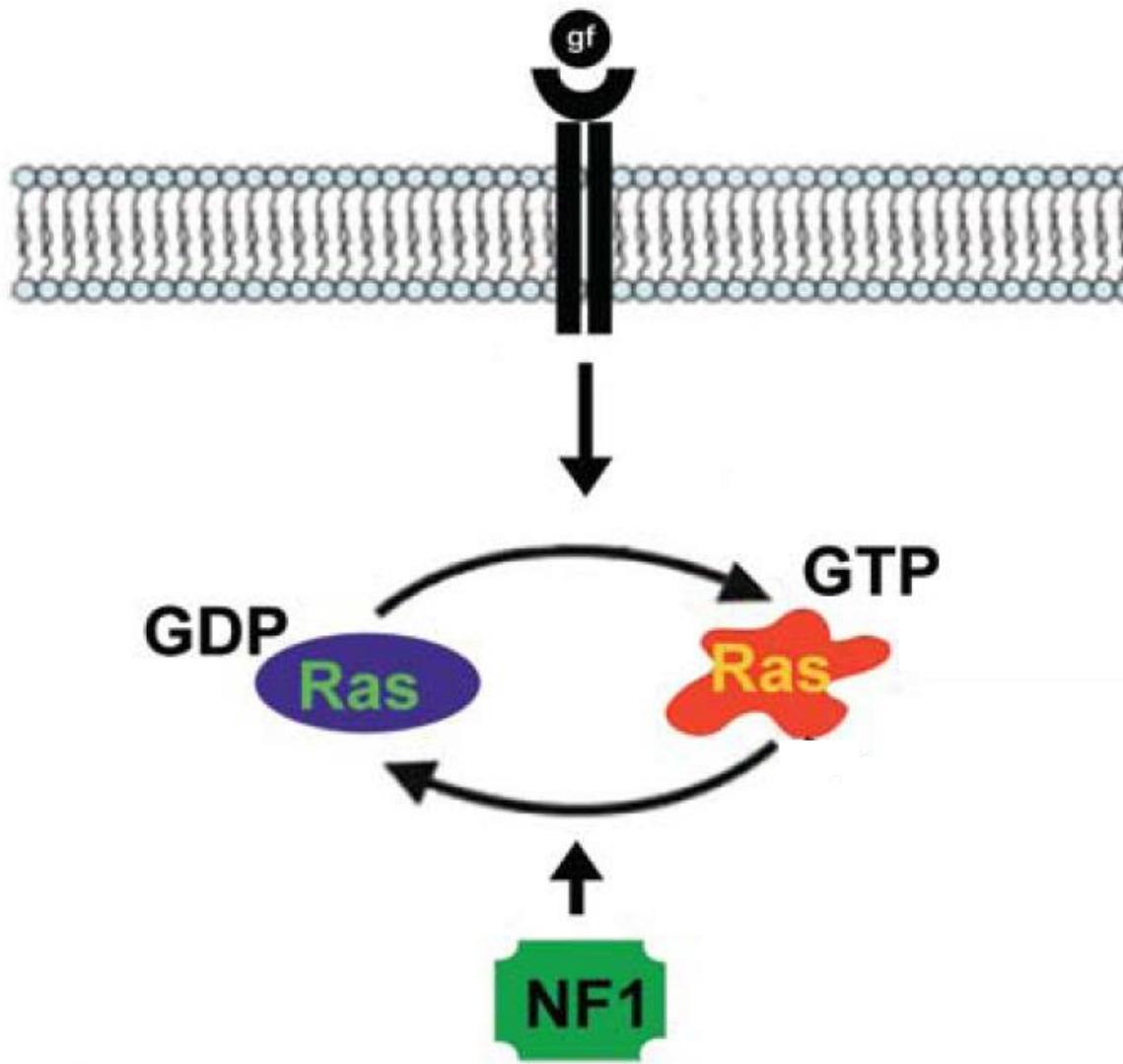
Neurofibromin 1

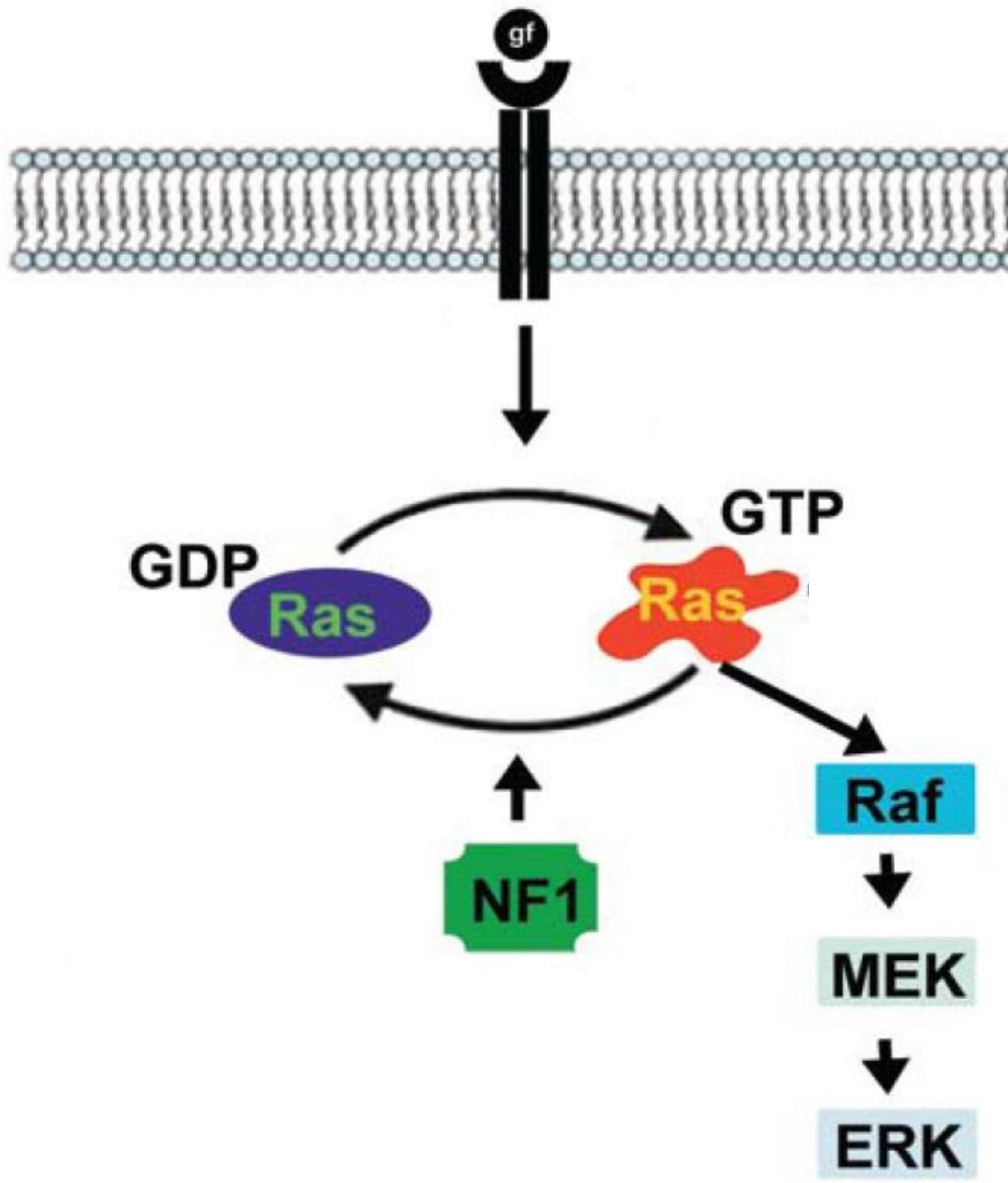
NF1

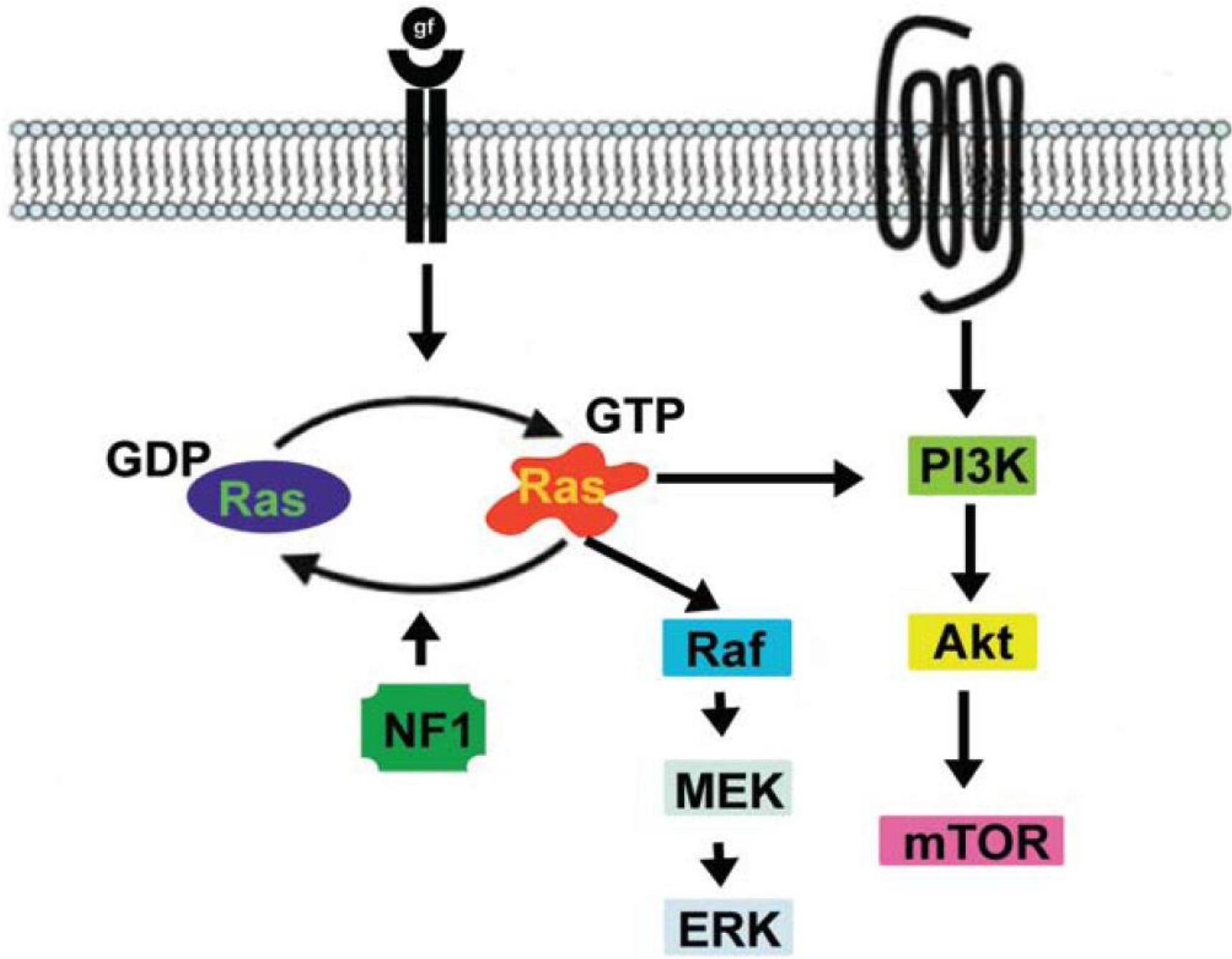


NF1





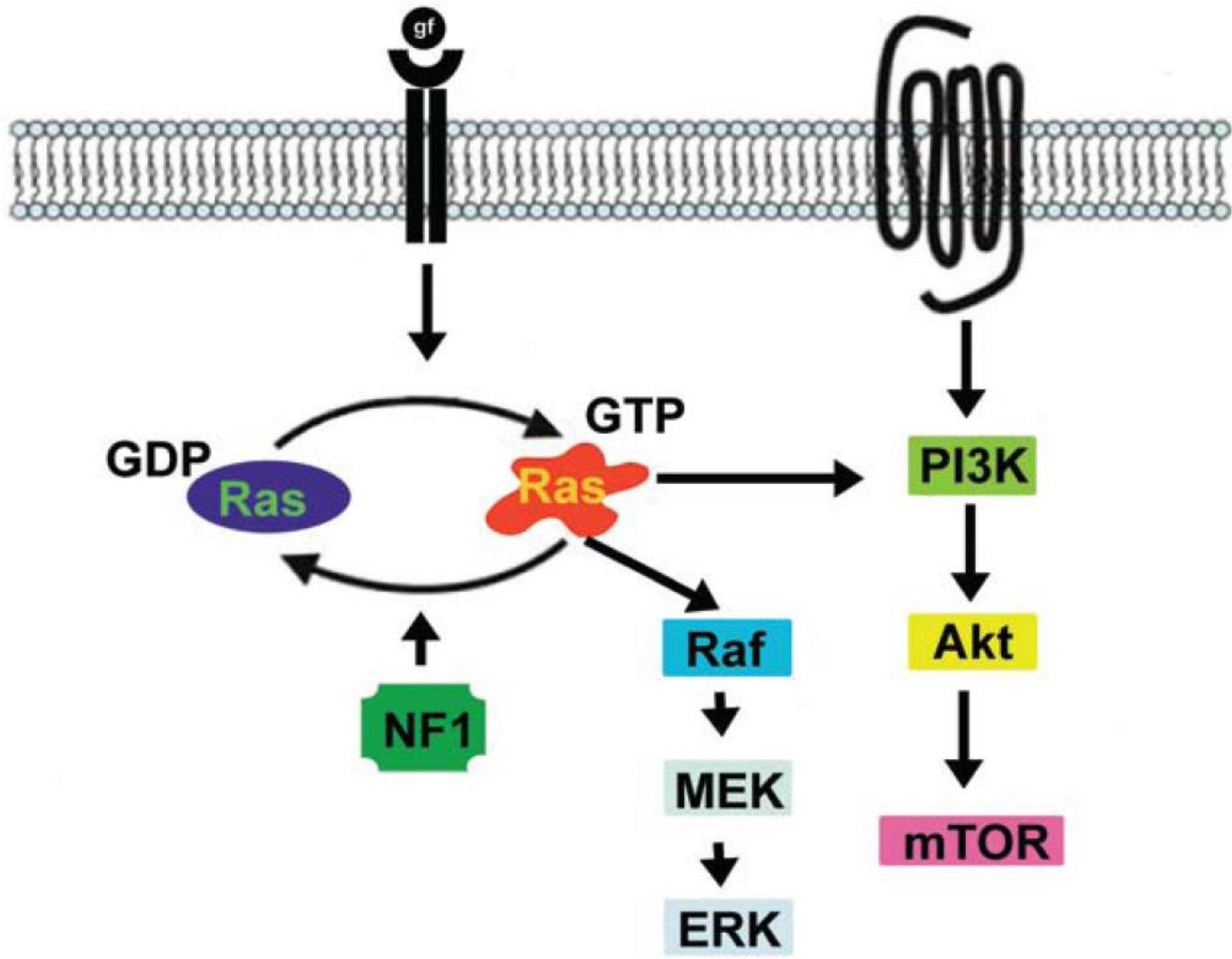






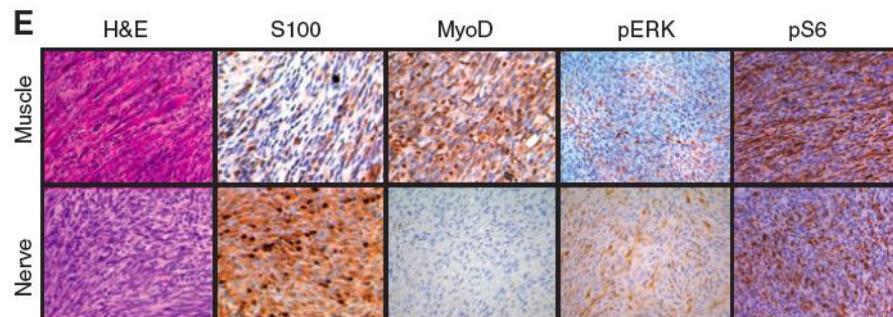
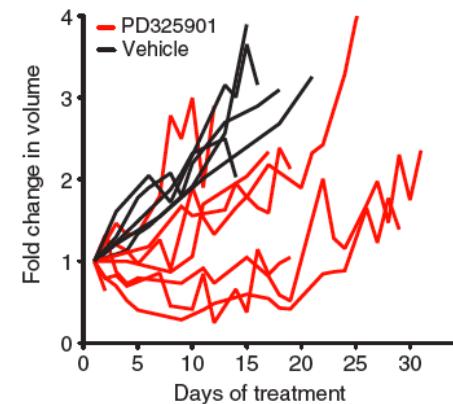
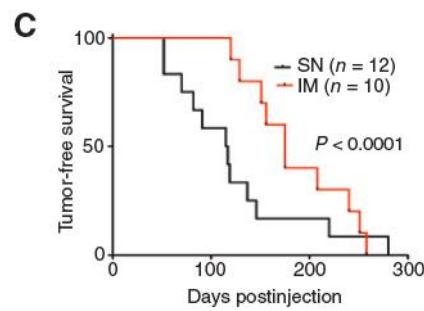
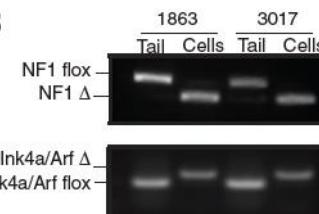
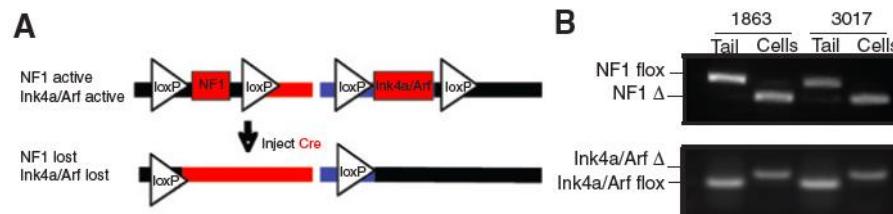
Where is Wally NF1?





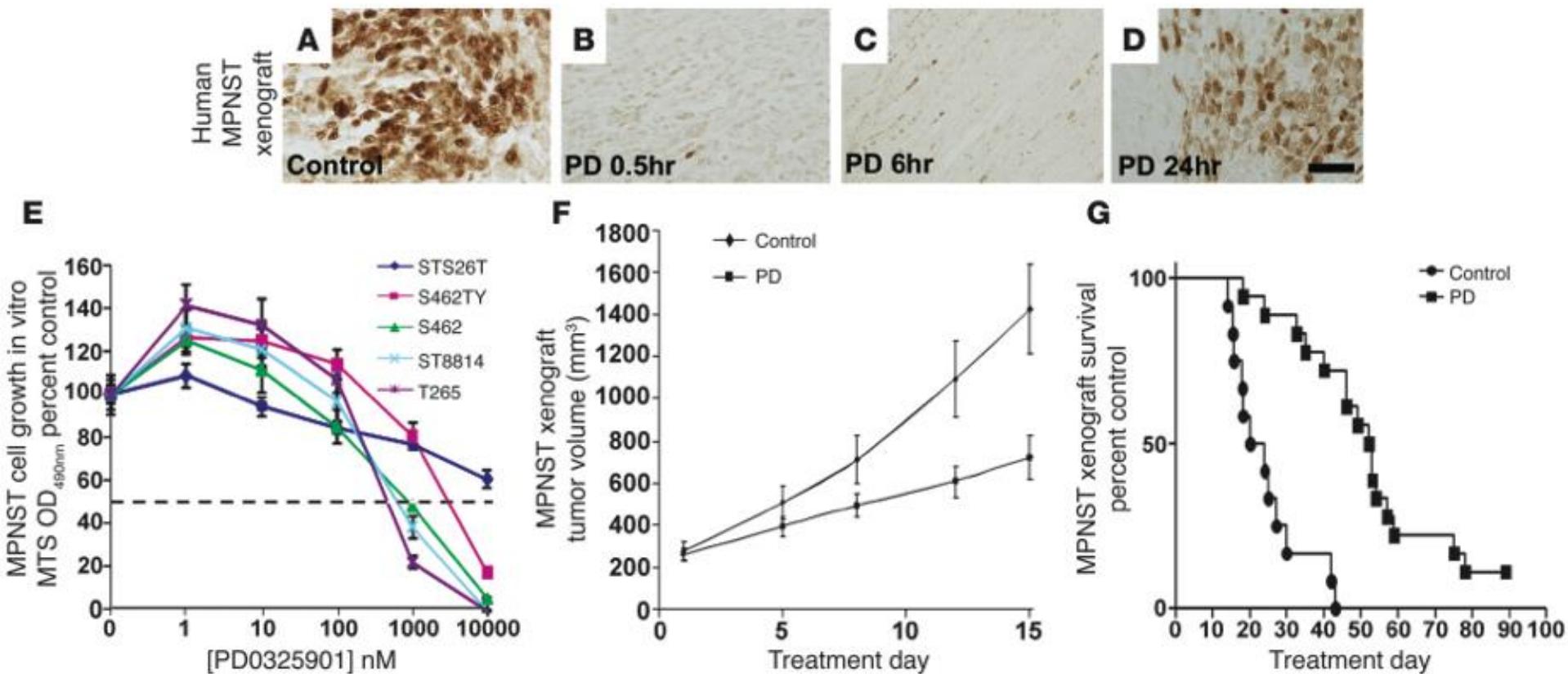
NF1 Deletion Generates Multiple Subtypes of Soft-Tissue Sarcoma That Respond to MEK Inhibition

Rebecca D. Dodd¹, Jeffrey K. Mito², William C. Eward³, Rhea Chitalia¹, Mohit Sachdeva¹, Yan Ma¹, Jordi Barretina^{5,6,7}, Leslie Dodd⁴, and David G. Kirsch^{1,2}

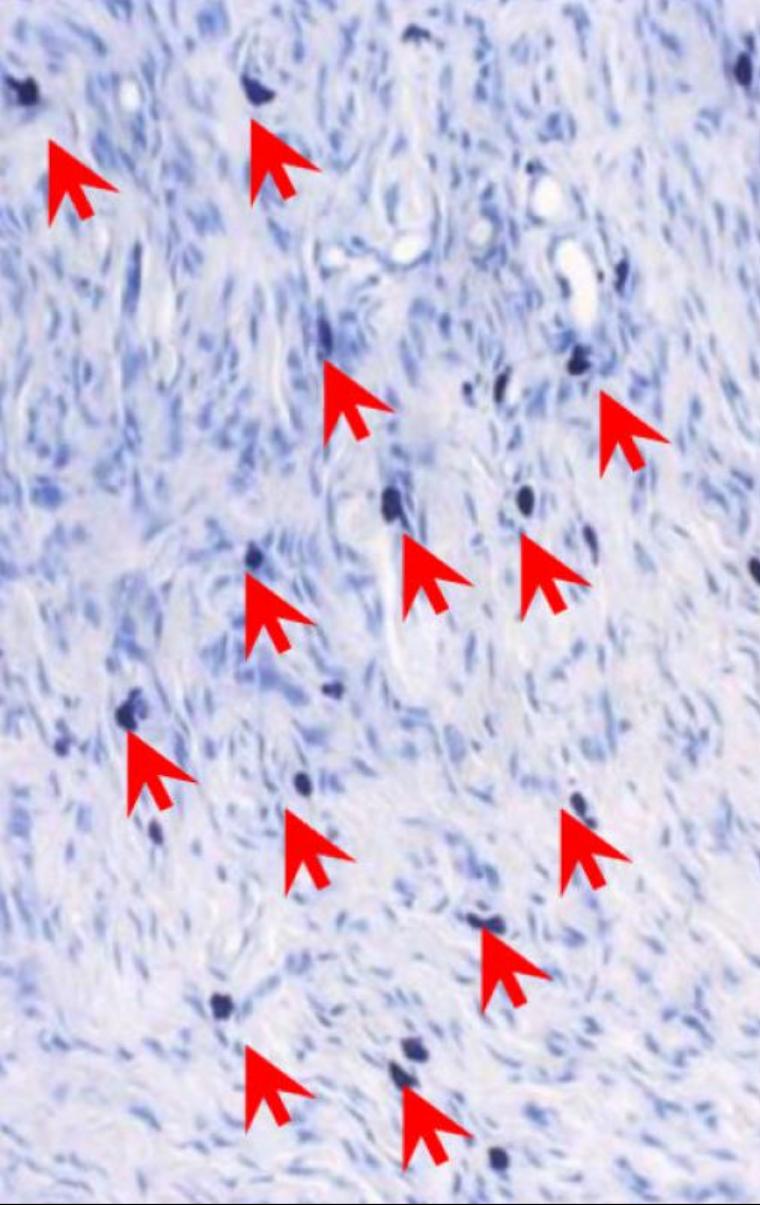


Mol Cancer Ther. 2013 Sep;12(9):1906-17

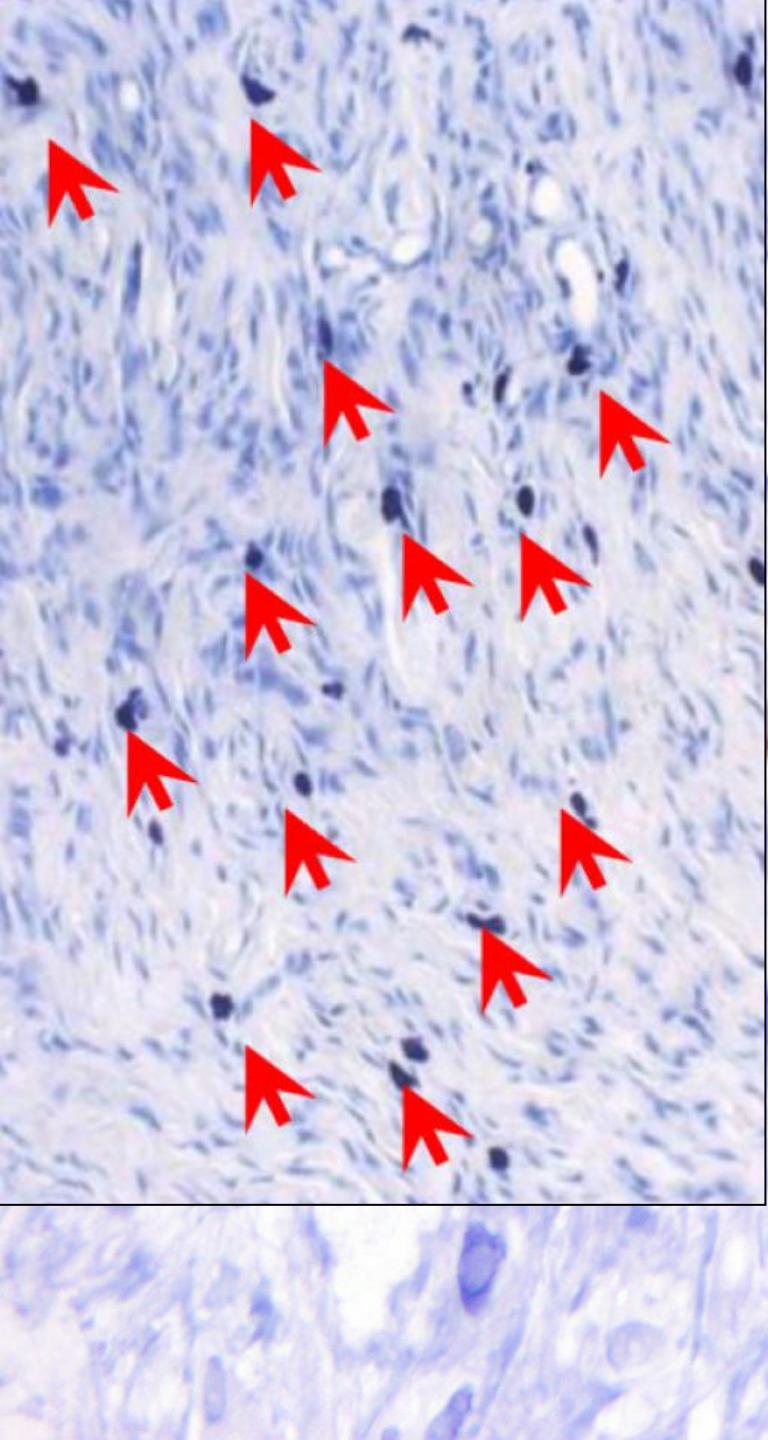
MEK inhibition exhibits efficacy in human and mouse neurofibromatosis tumors



Jessen et al *J Clin Invest.* 2013;123(1):340–34

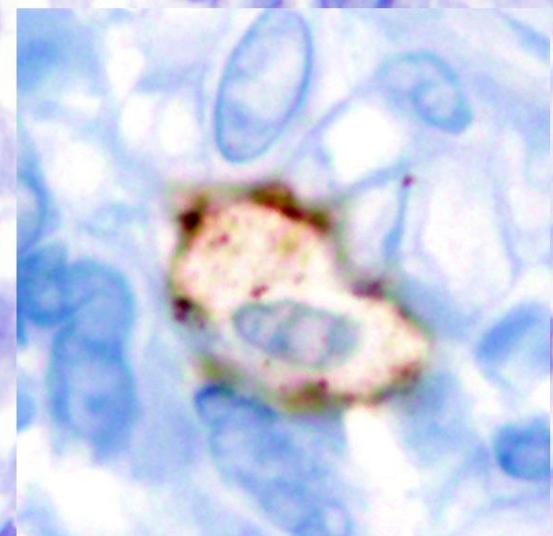


Neurofibroma

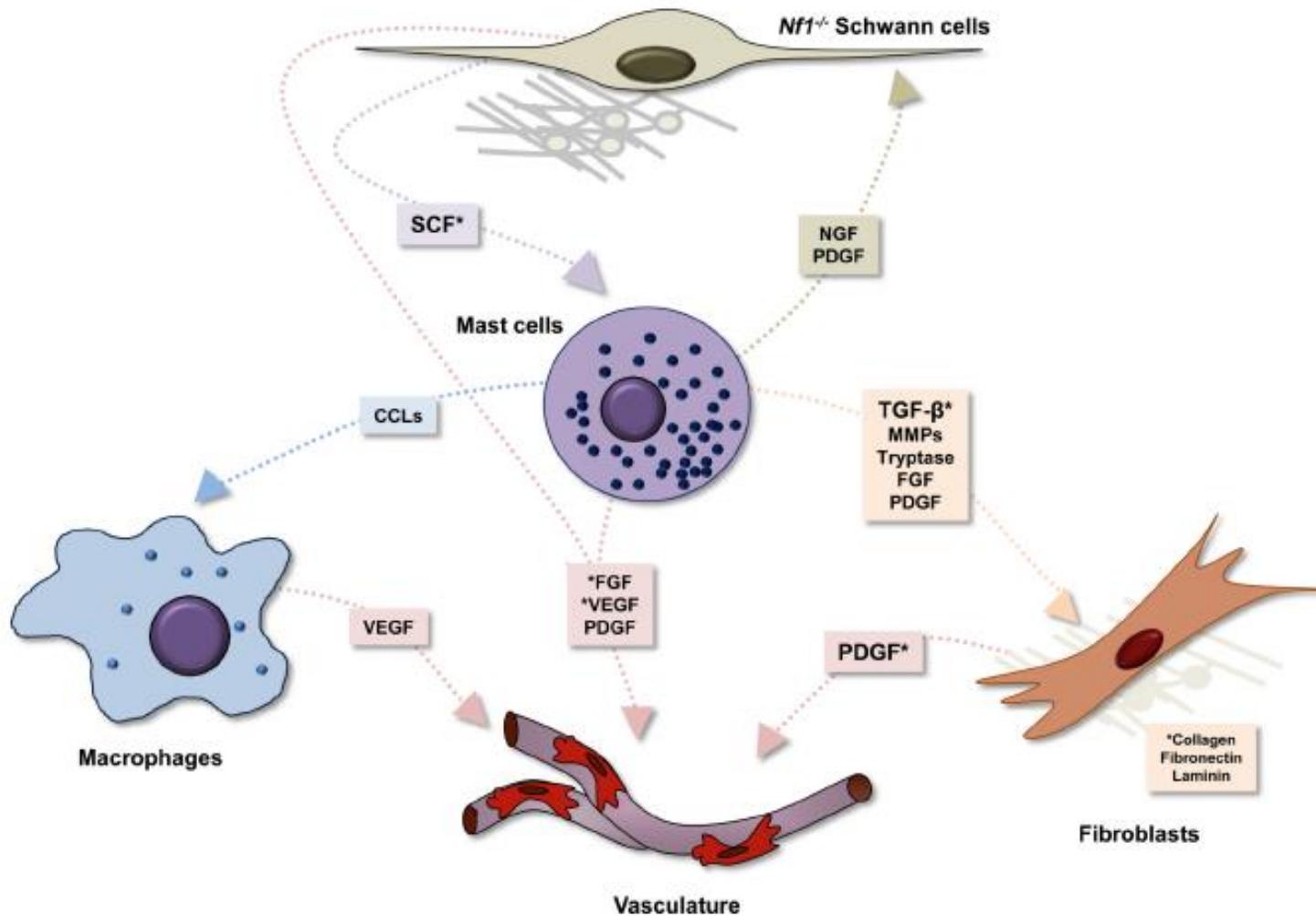


Neurofibroma
CD117 (KIT)

This image shows immunohistochemical staining of a neurofibroma tissue sample. The background is stained blue, likely with hematoxylin. Red arrowheads point to several cells showing brown staining, indicating the presence of the CD117 (KIT) protein. An inset image in the bottom right corner provides a higher magnification view of a single cell with prominent brown staining.



Tumor/stromal interactions in neurofibroma microenvironment



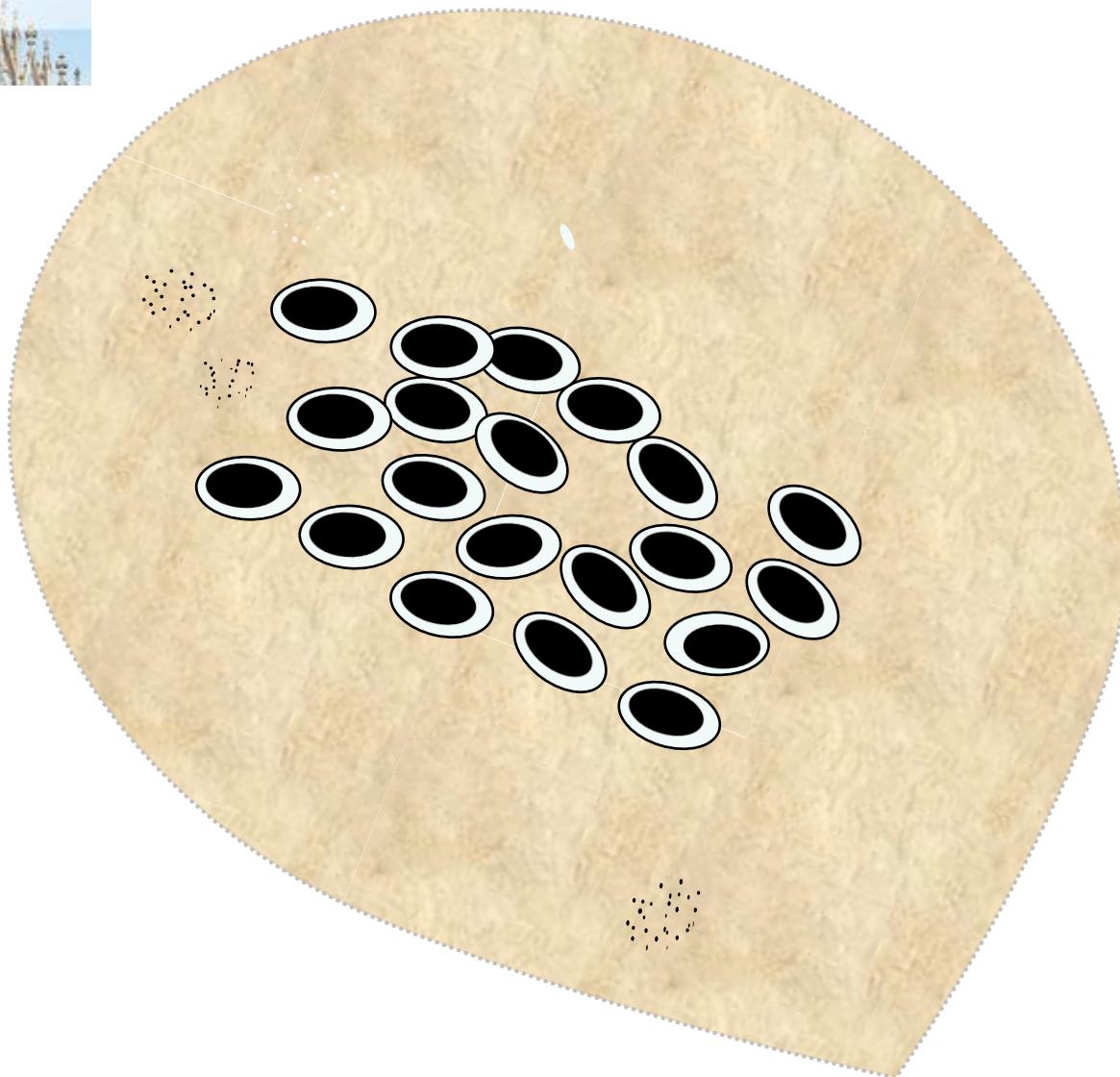


Sarcoma and GIST
Conference 2014

18-19 February 2014, Milan, Italy

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BEST PRACTICE

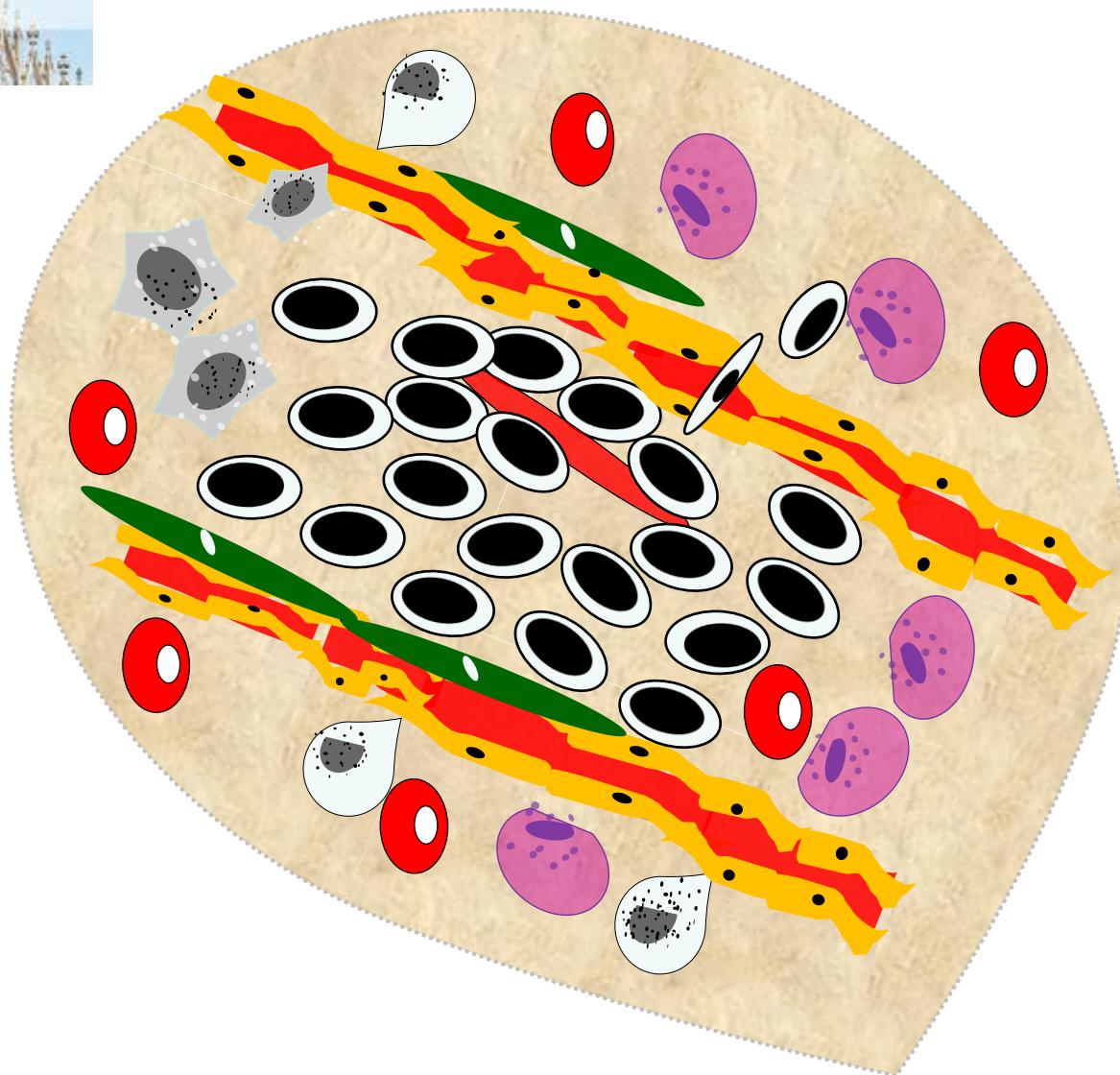
European Society for Medical Oncology



18-19 February 2014, Milan, Italy

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BETTER MEDICINE
BEST PRACTICE

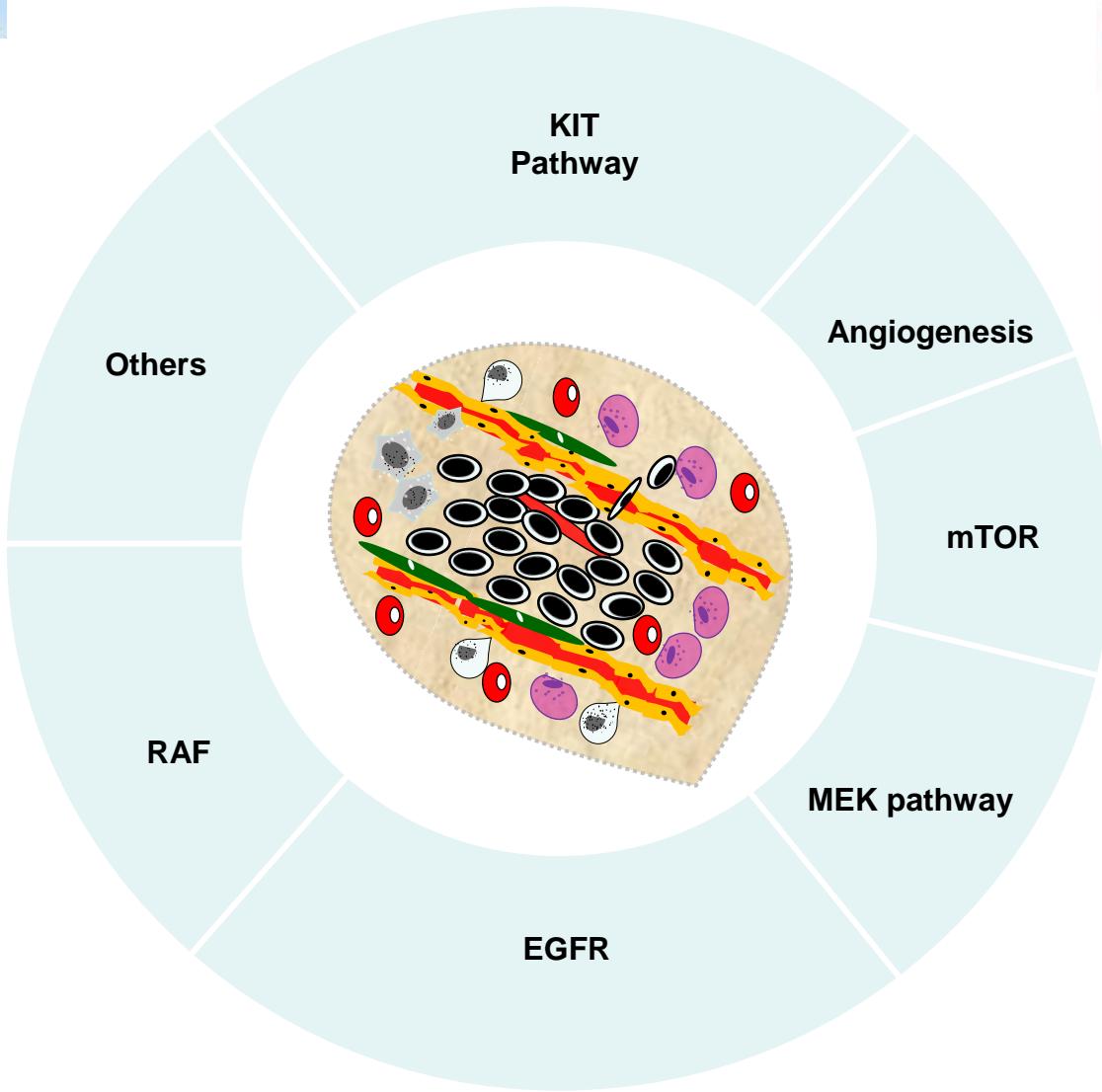
European Society for Medical Oncology



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European Society for Medical Oncology



Nilotinib

Imatinib

HDAC I
HSP90
Survivin
WNT pathway
AURKA

Others

RAF

KIT
Pathway

EGFR

Angiogenesis

mTOR

MEK pathway

Sorafenib

AZD6244

Erlotinib

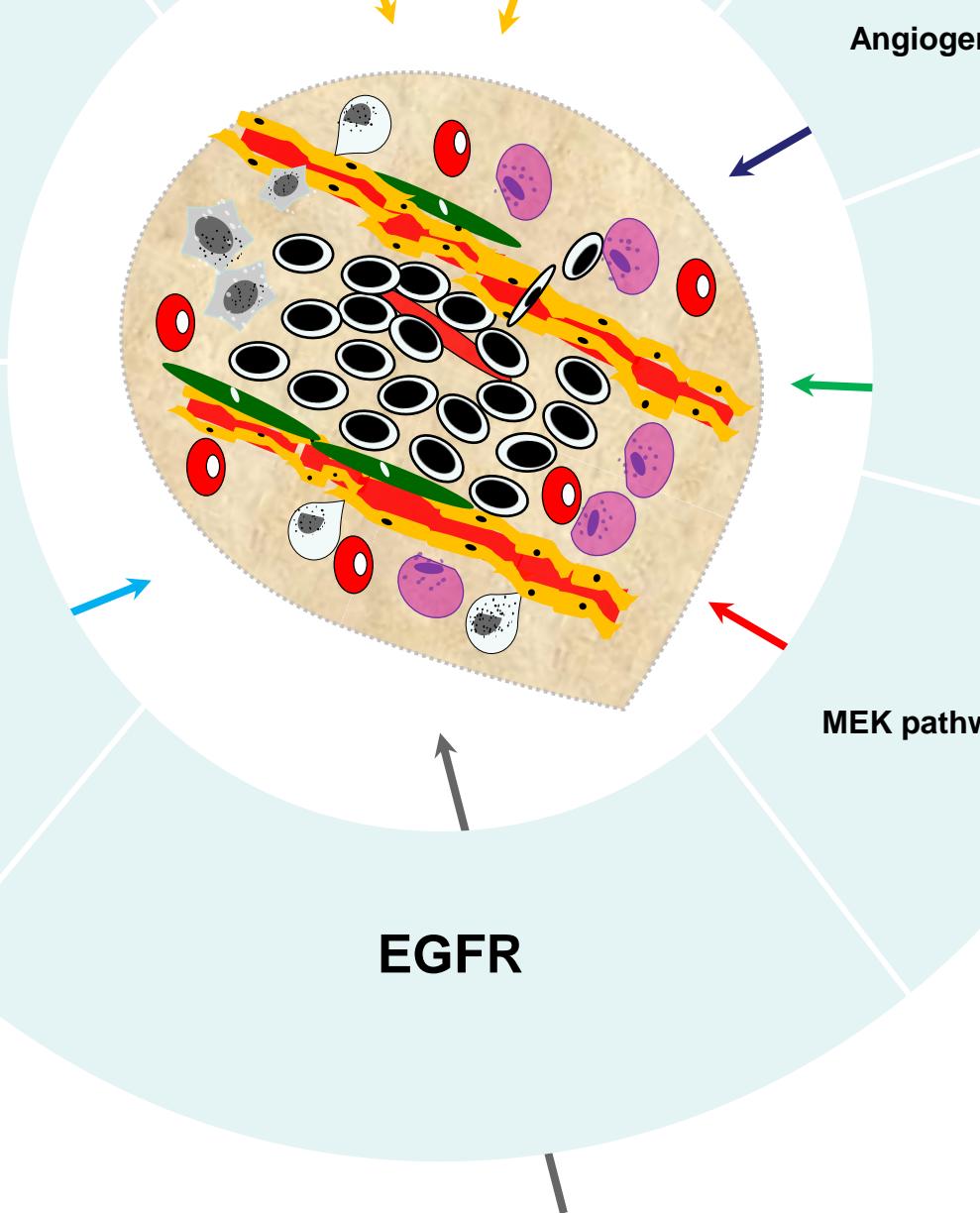
Bevacizumab

Everolimus



Angio

Others



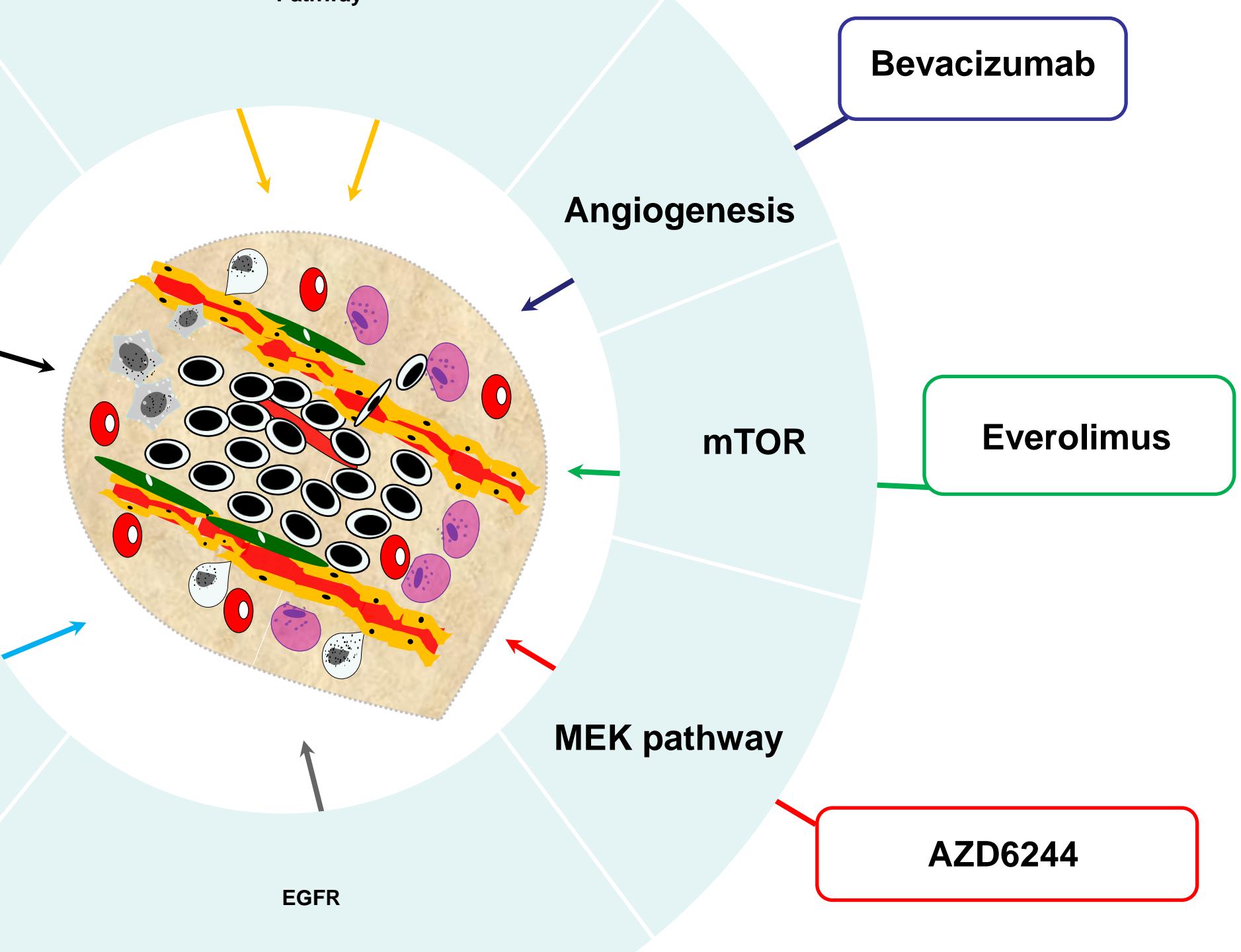
~~Sorafenib~~

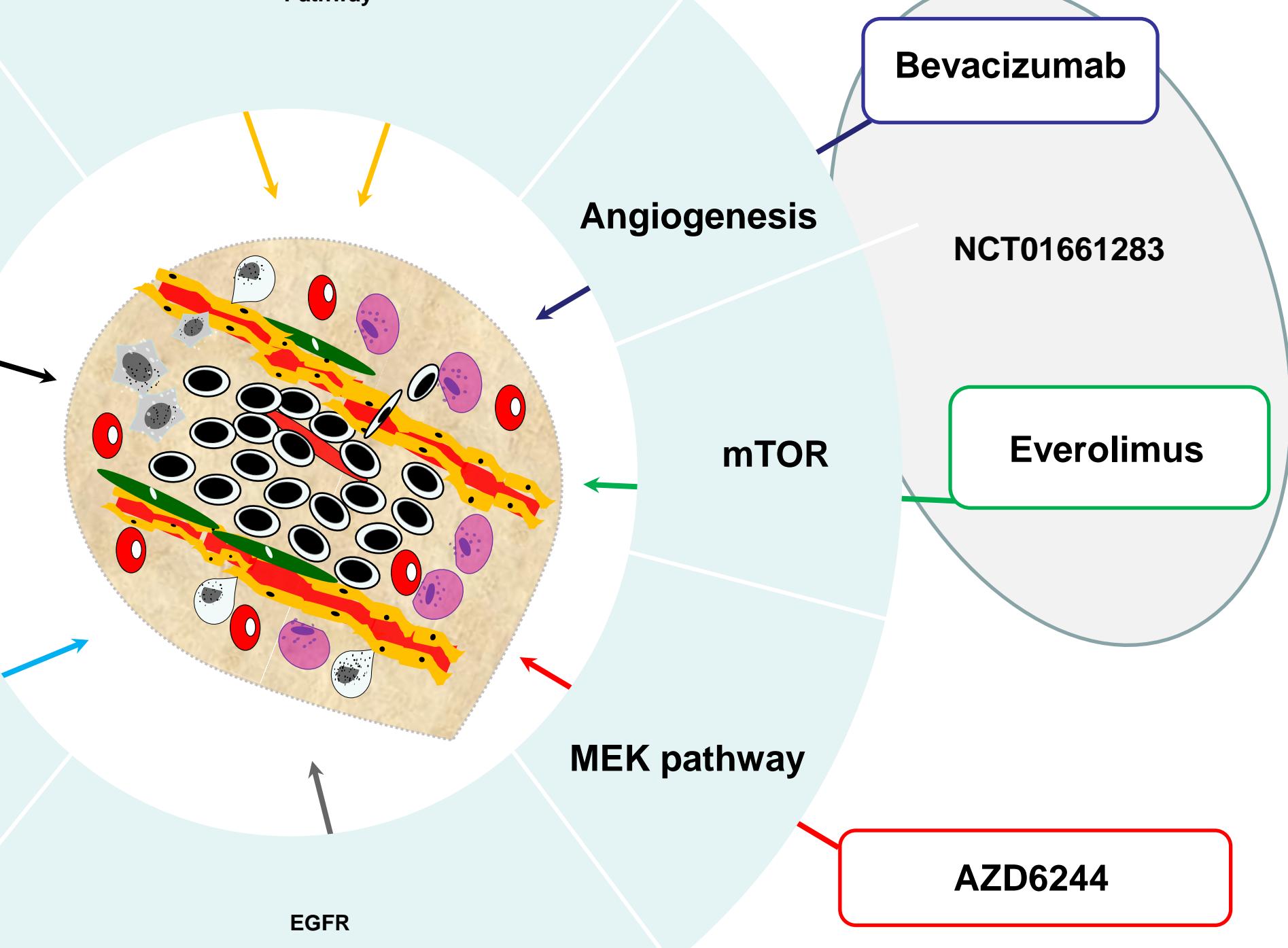
EGFR

~~Erlotinib~~

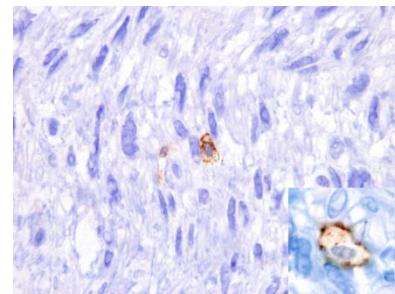
DOO SCIENCE
CLINIC MEDICINE
EST PRACTICE

European Society for Medical Oncology



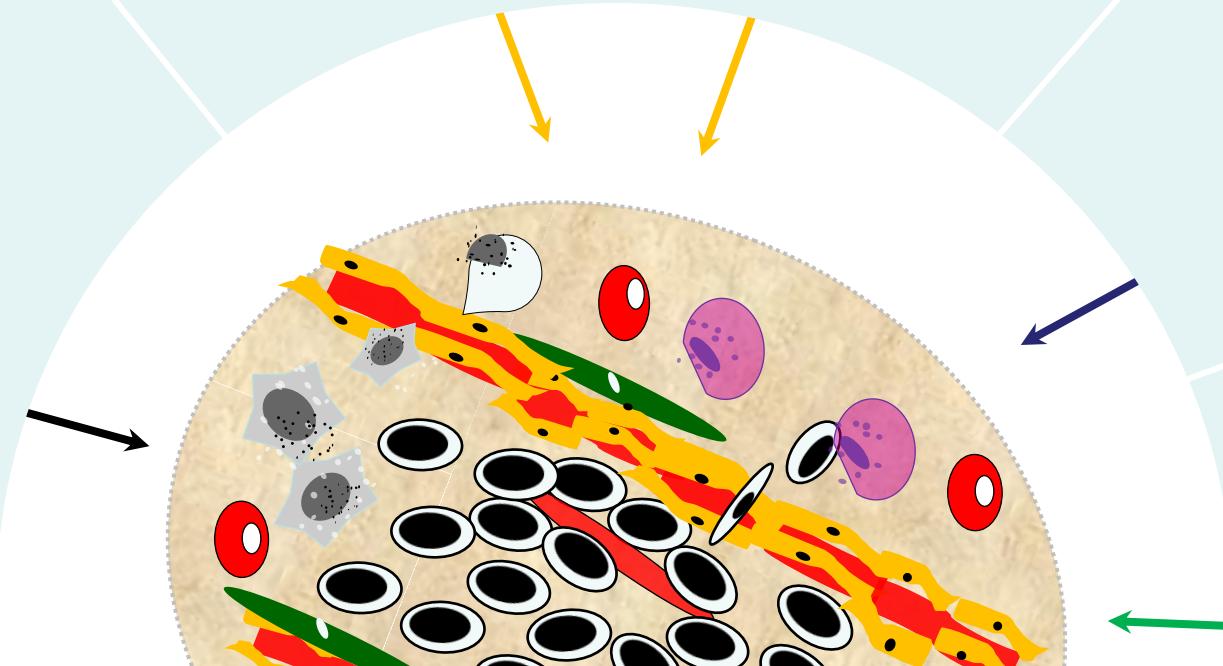


Nilotinib



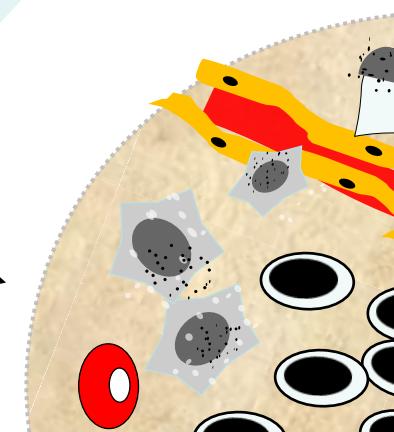
Imatinib

KIT Pathway



**HDAC i
HSP90
Survivin
WNT pathway
AURKA**

Others



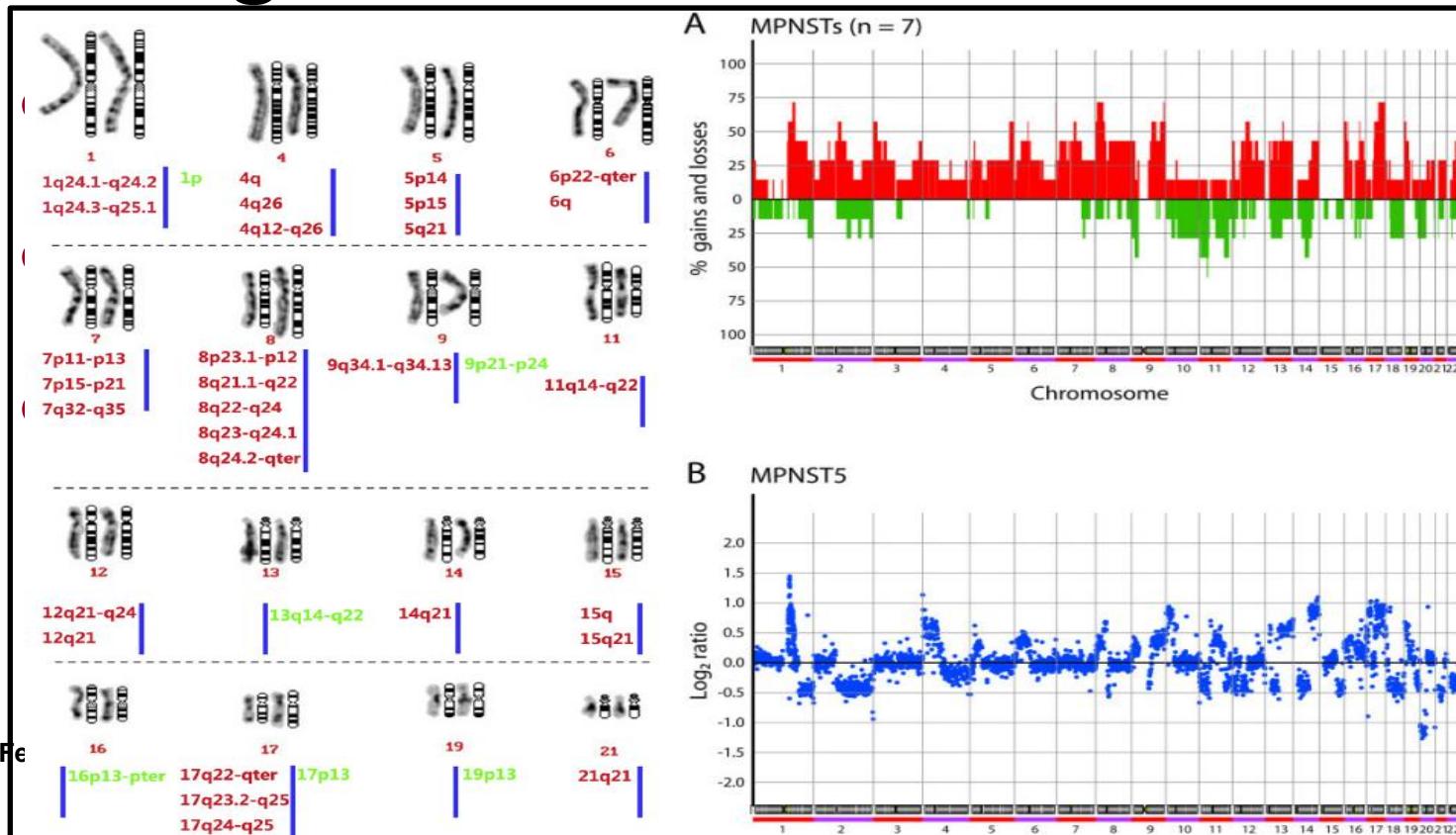
Challenges

- Tumor heterogeneity (inter/intra)



Challenges

- Tumor heterogeneity (inter/intra)
- Progression NF1 -->MPNST



Challenges

- Tumor heterogeneity (inter/intra)
- Progression NF1 -->MPNST
- MPNST not related to NF1
- Multicenter collaboration
- Innovative design of clinical trials



thank you

JaviNavarro.es

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NF1 mutations are common

- MPNST
- Myxofibrosarcoma (4+/35)
- pleomorphic liposarcoma (2+/24)
- GIST (also somatic BRAF, KRAS)