

The biology of malignant peripheral nerve sheath tumours

Enrique de Alava

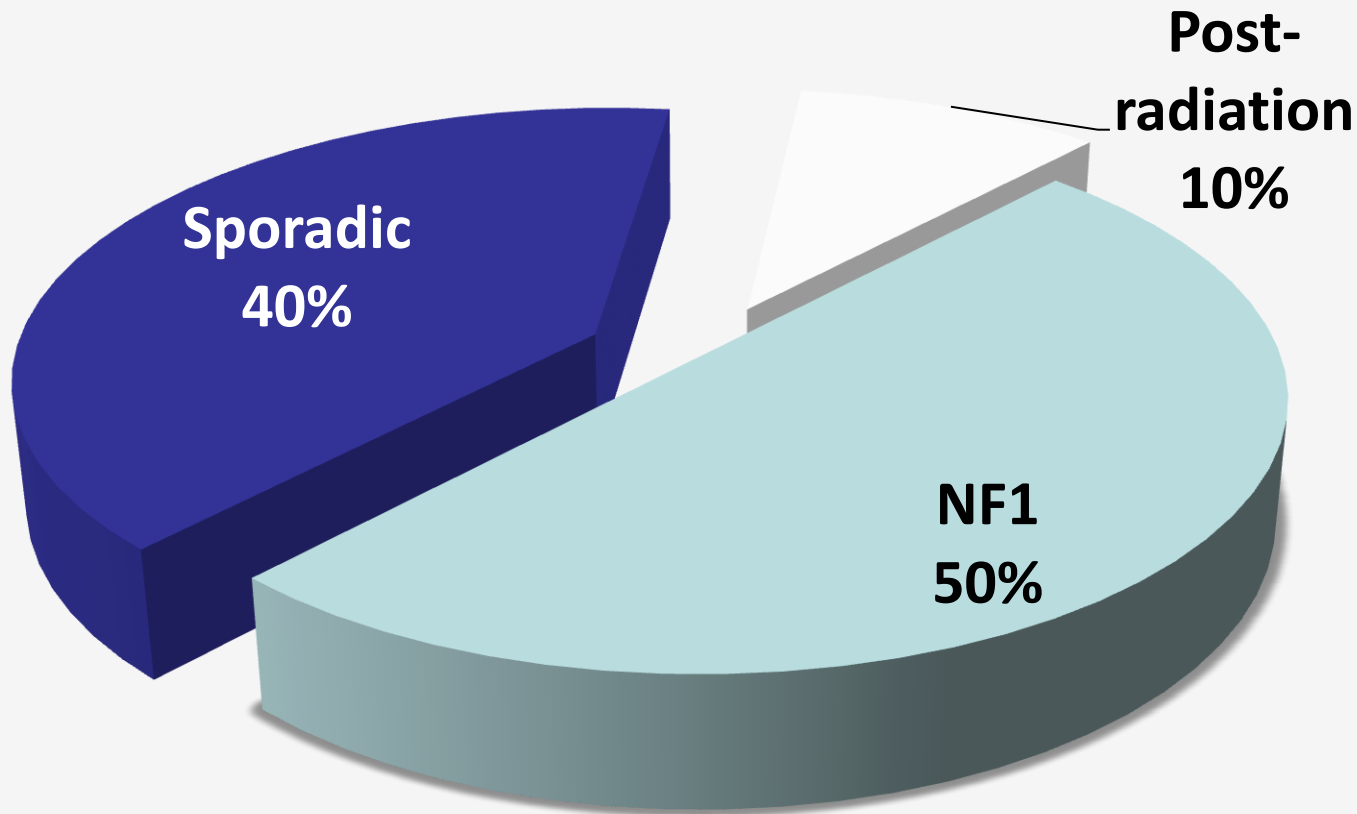


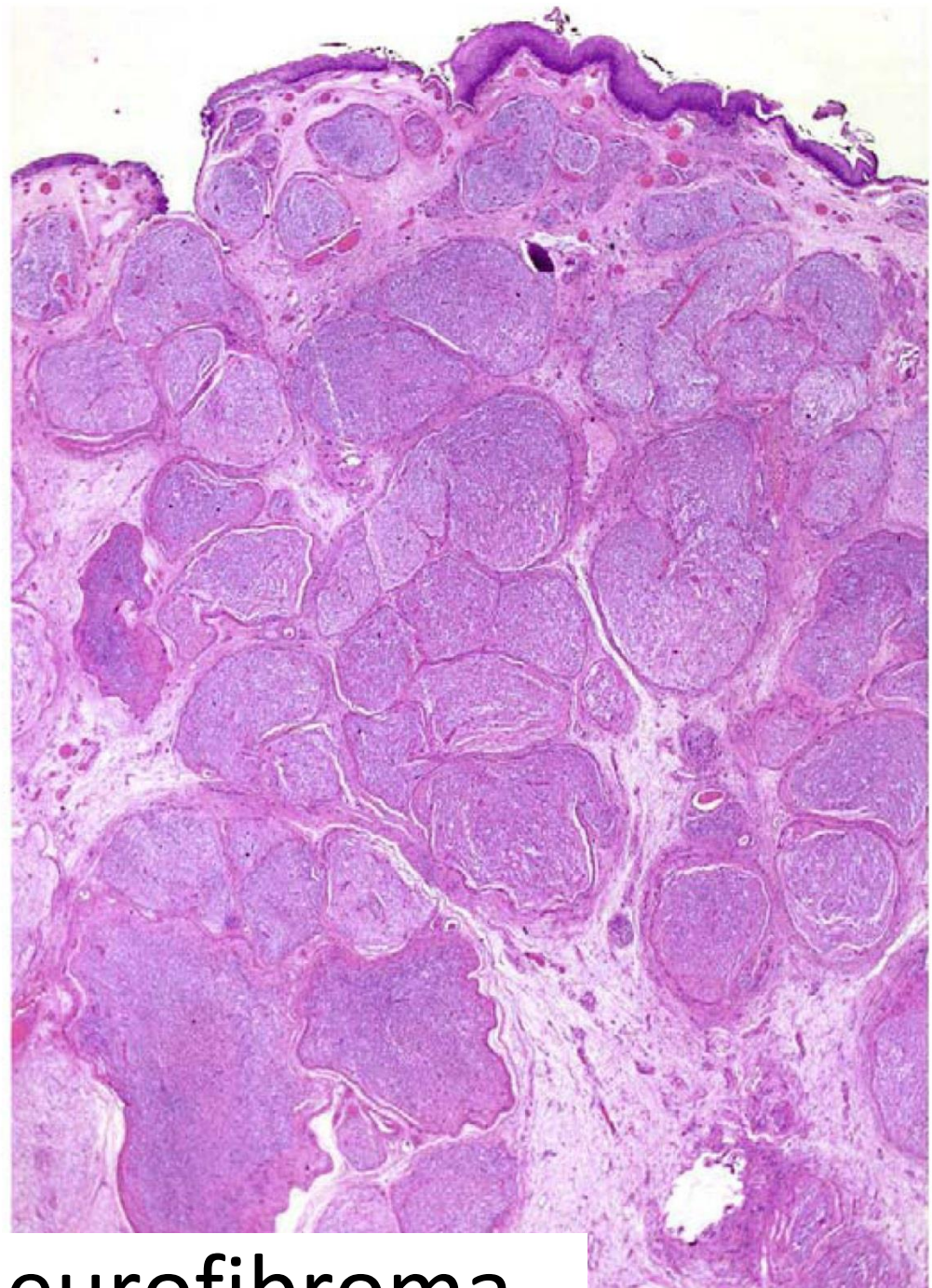
18-19 February 2014, Milan, Italy

Disclosure slide

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

Three clinical settings





Plexiform Neurofibroma

Neurofibromatosis type 1.

Neurofibromin 1

NF1

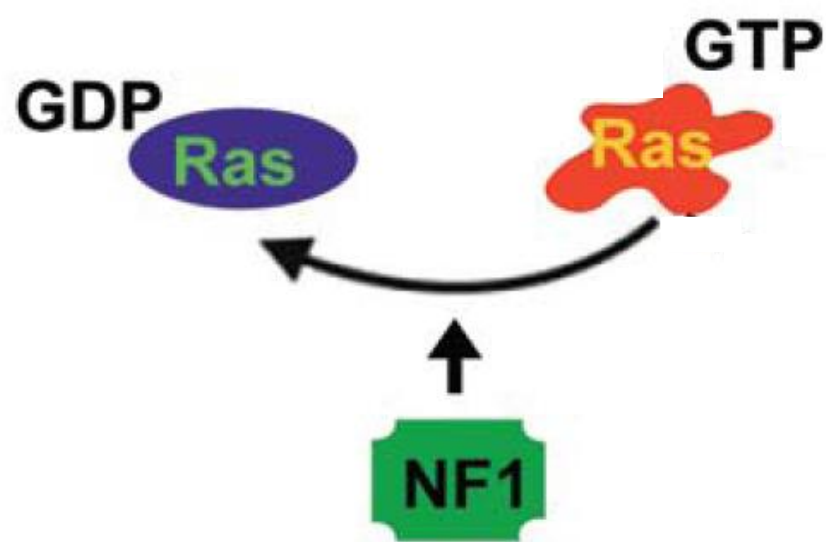
Neurofibromatosis type 1.

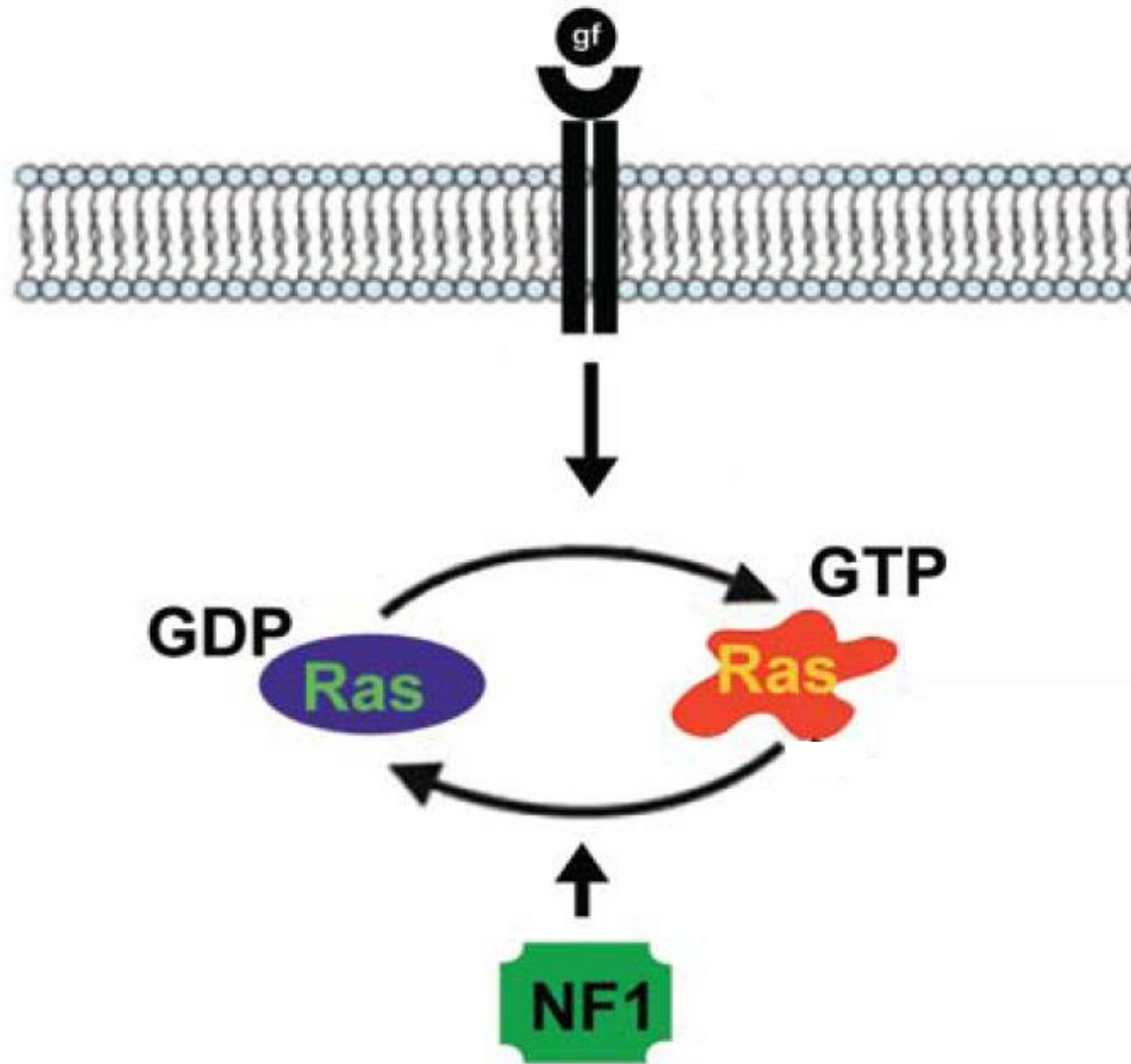
Neurofibromin 1

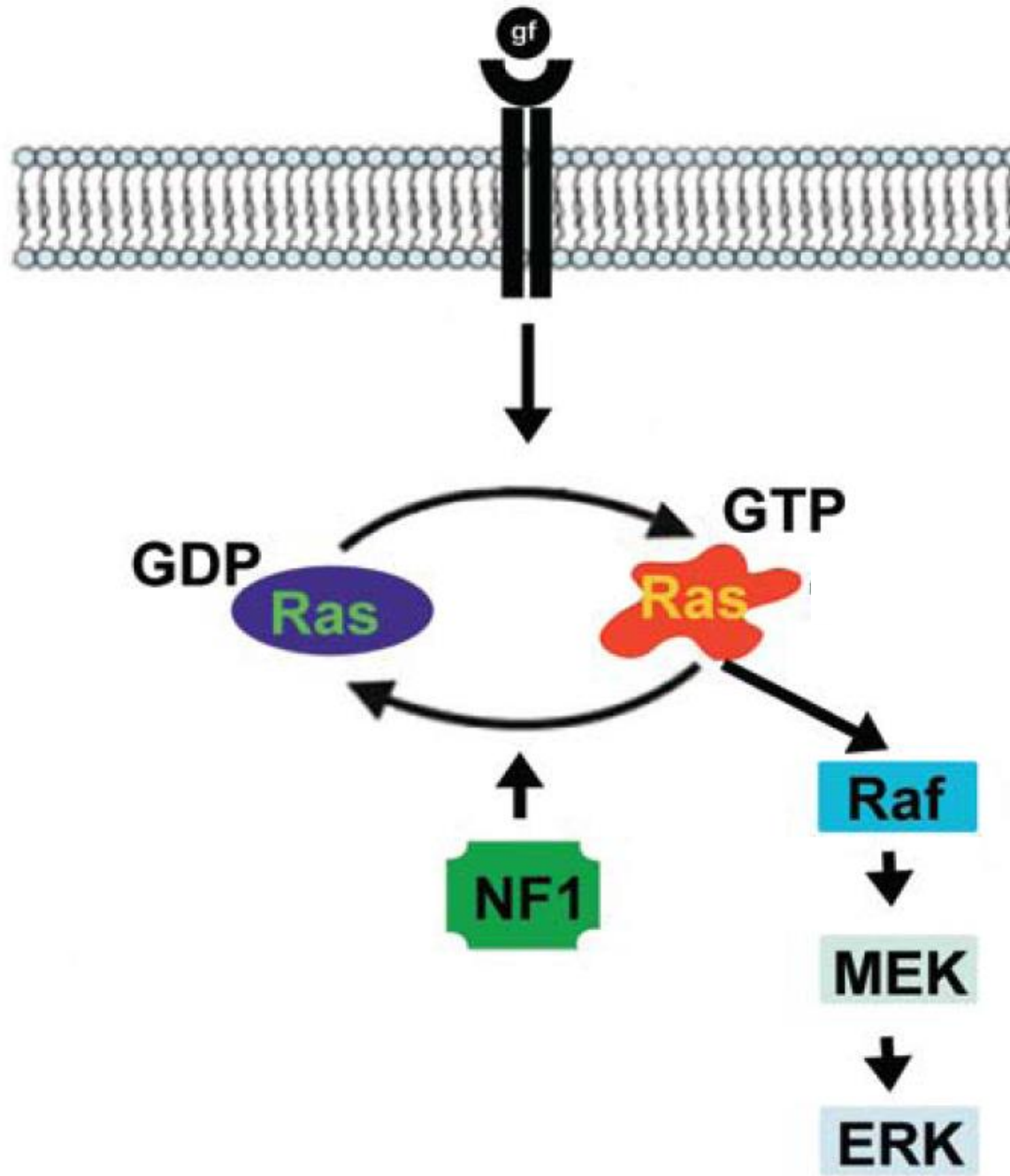
NF1

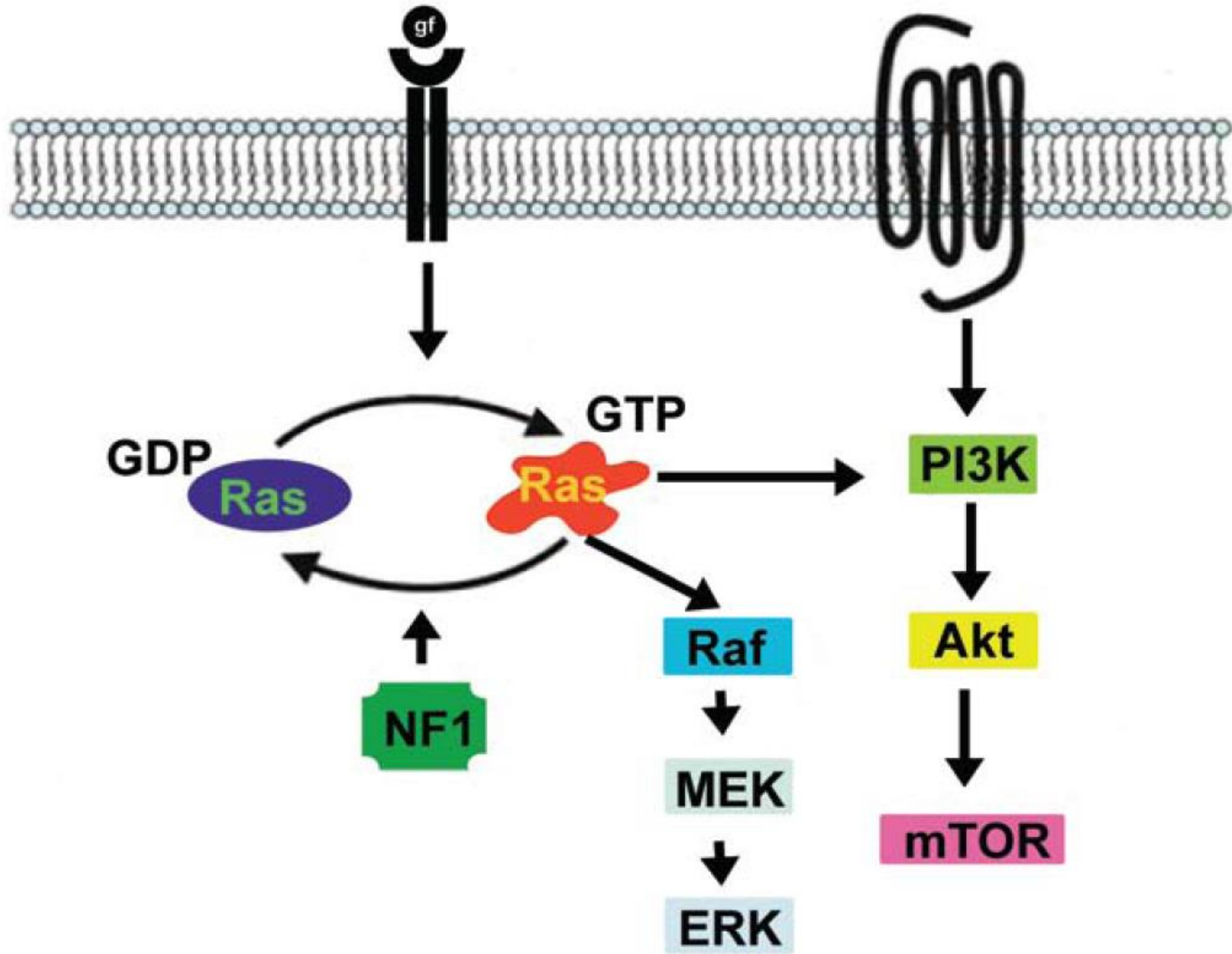






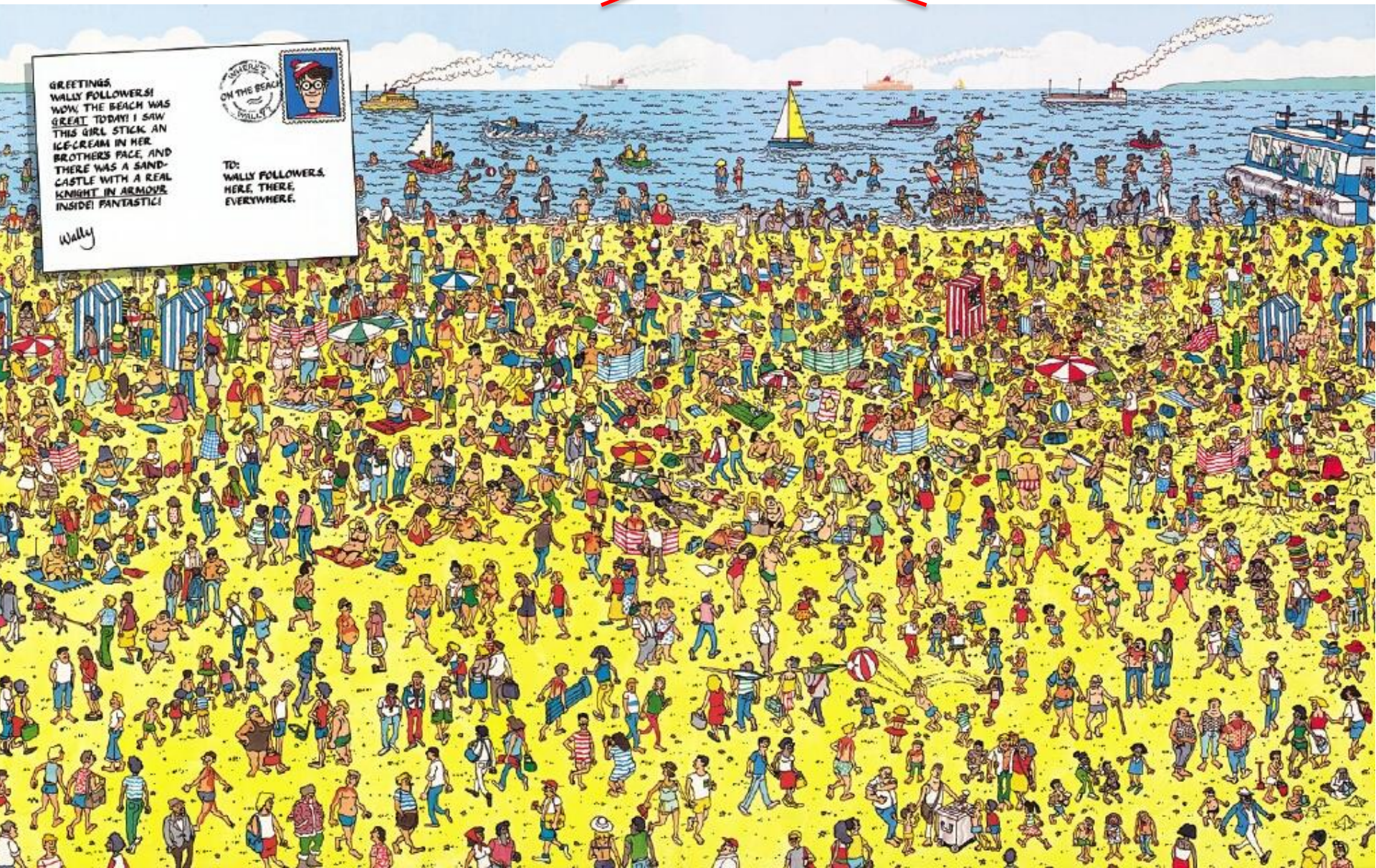


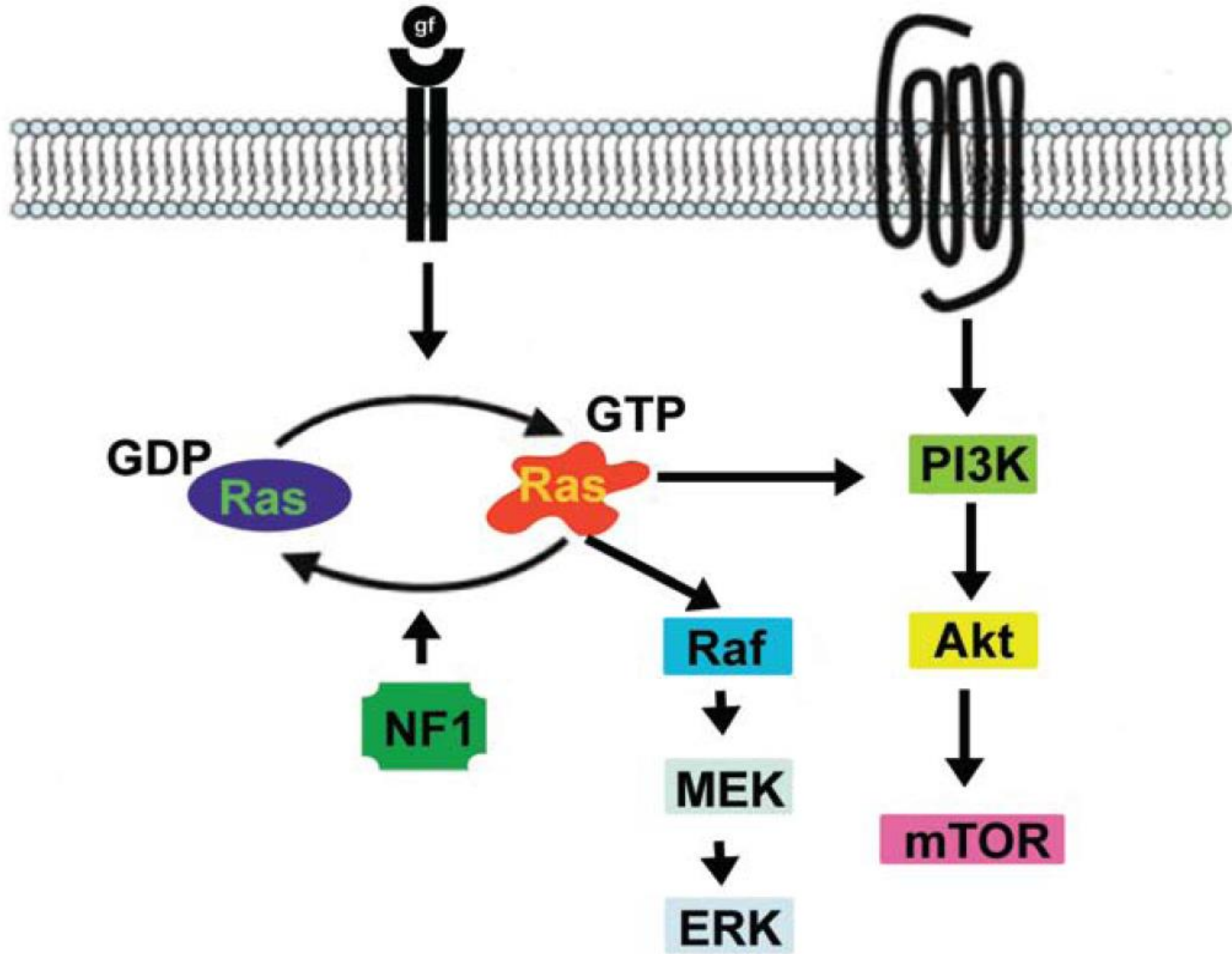






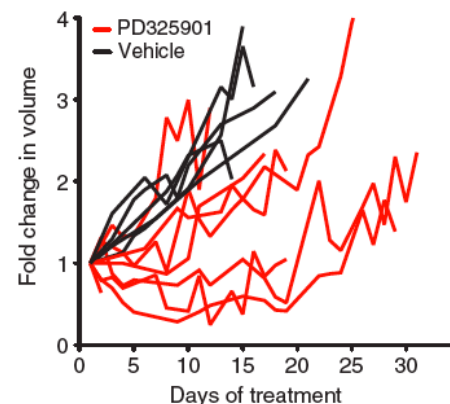
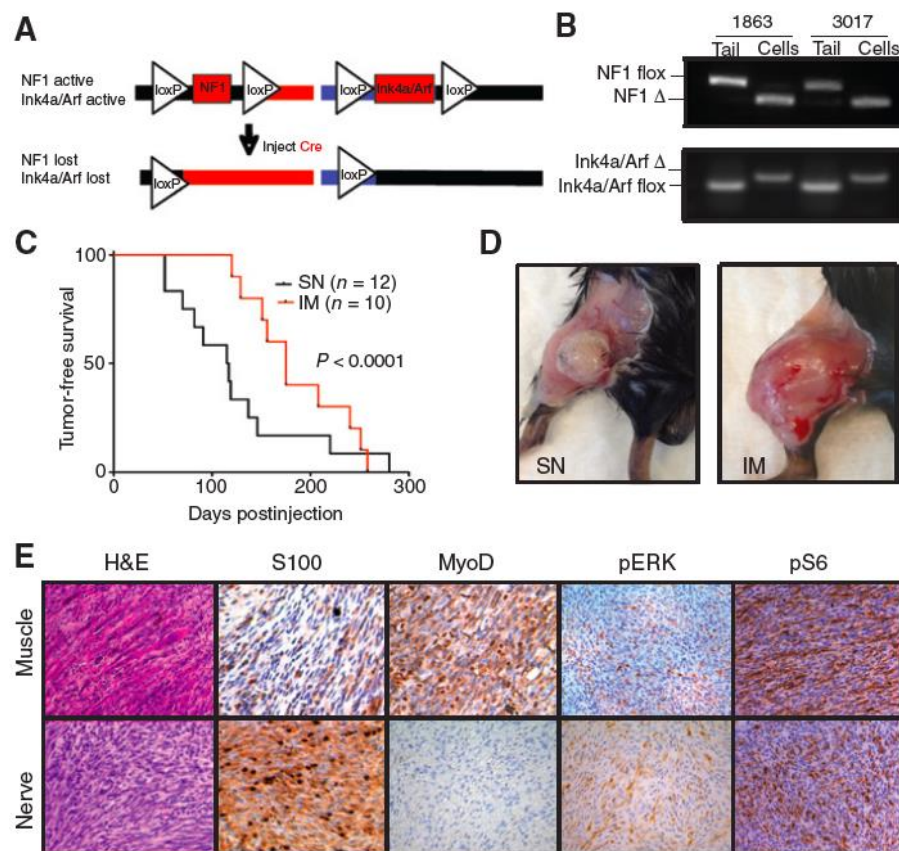
Where is ~~Wally~~ NF1?





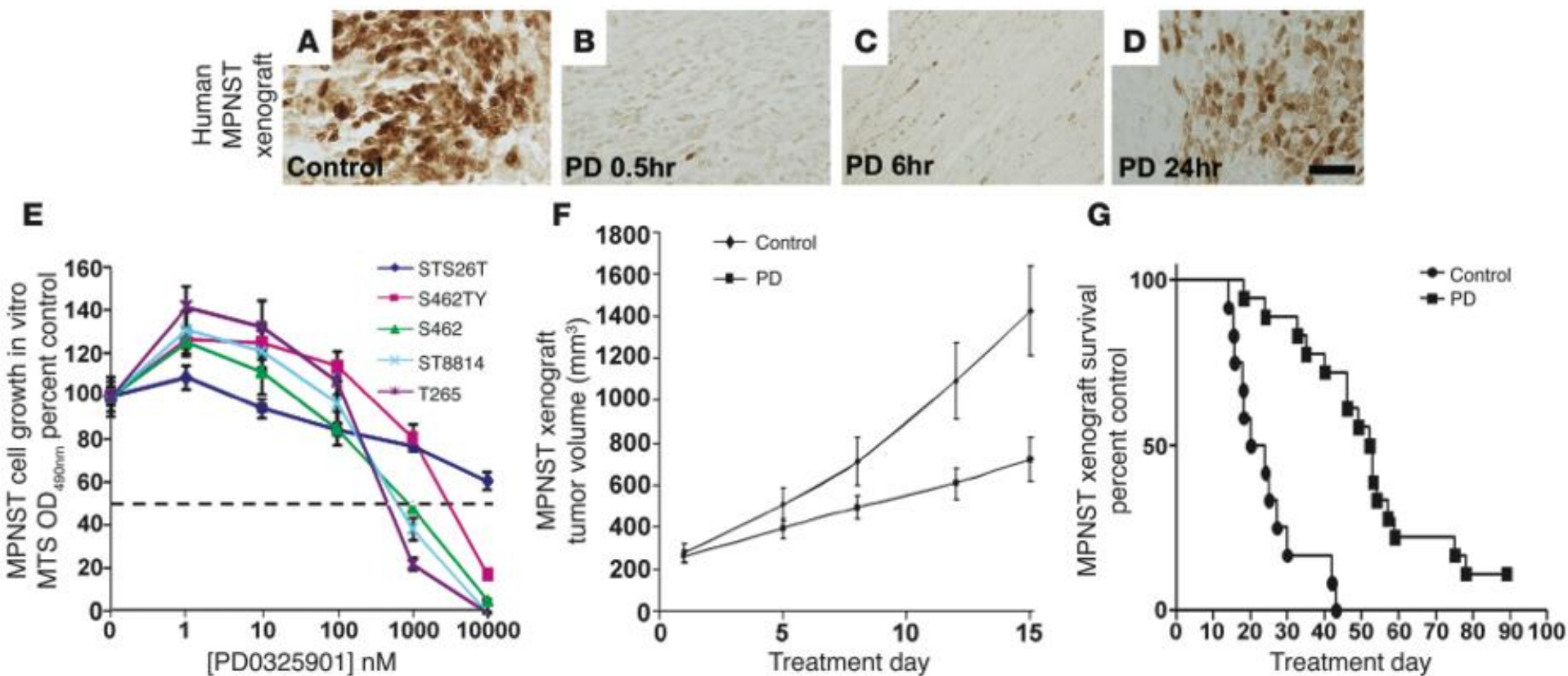
NF1 Deletion Generates Multiple Subtypes of Soft-Tissue Sarcoma That Respond to MEK Inhibition

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}



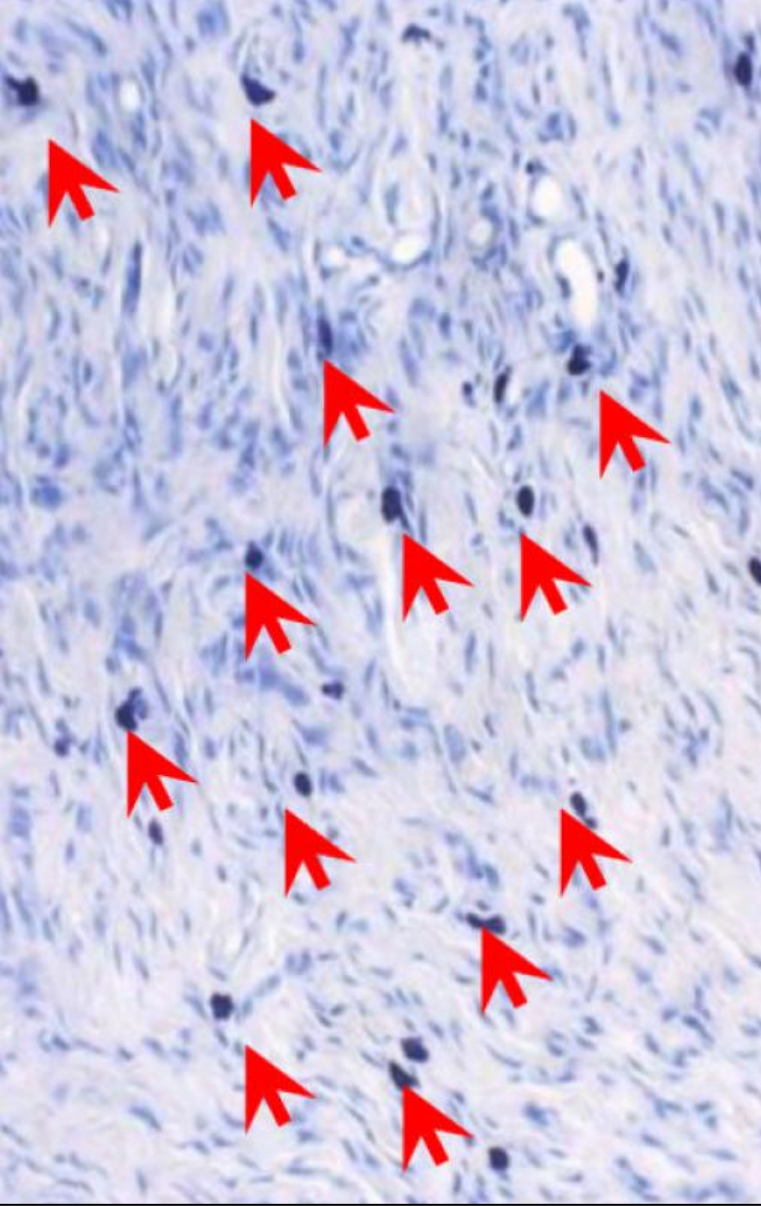
Mol Cancer Ther. 2013 Sep;12(9):1906-17

MEK inhibition exhibits efficacy in human and mouse neurofibromatosis tumors



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

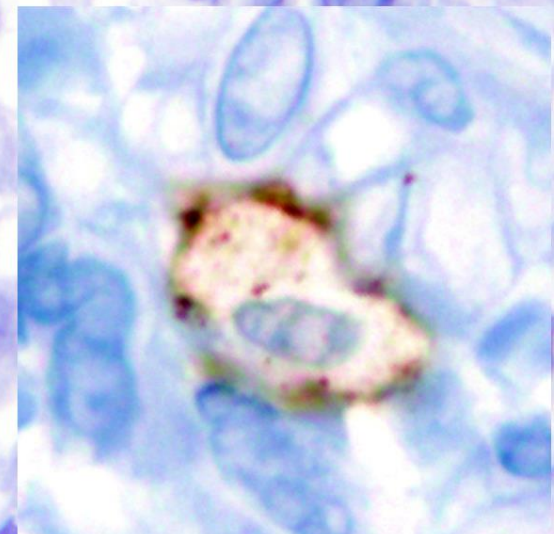
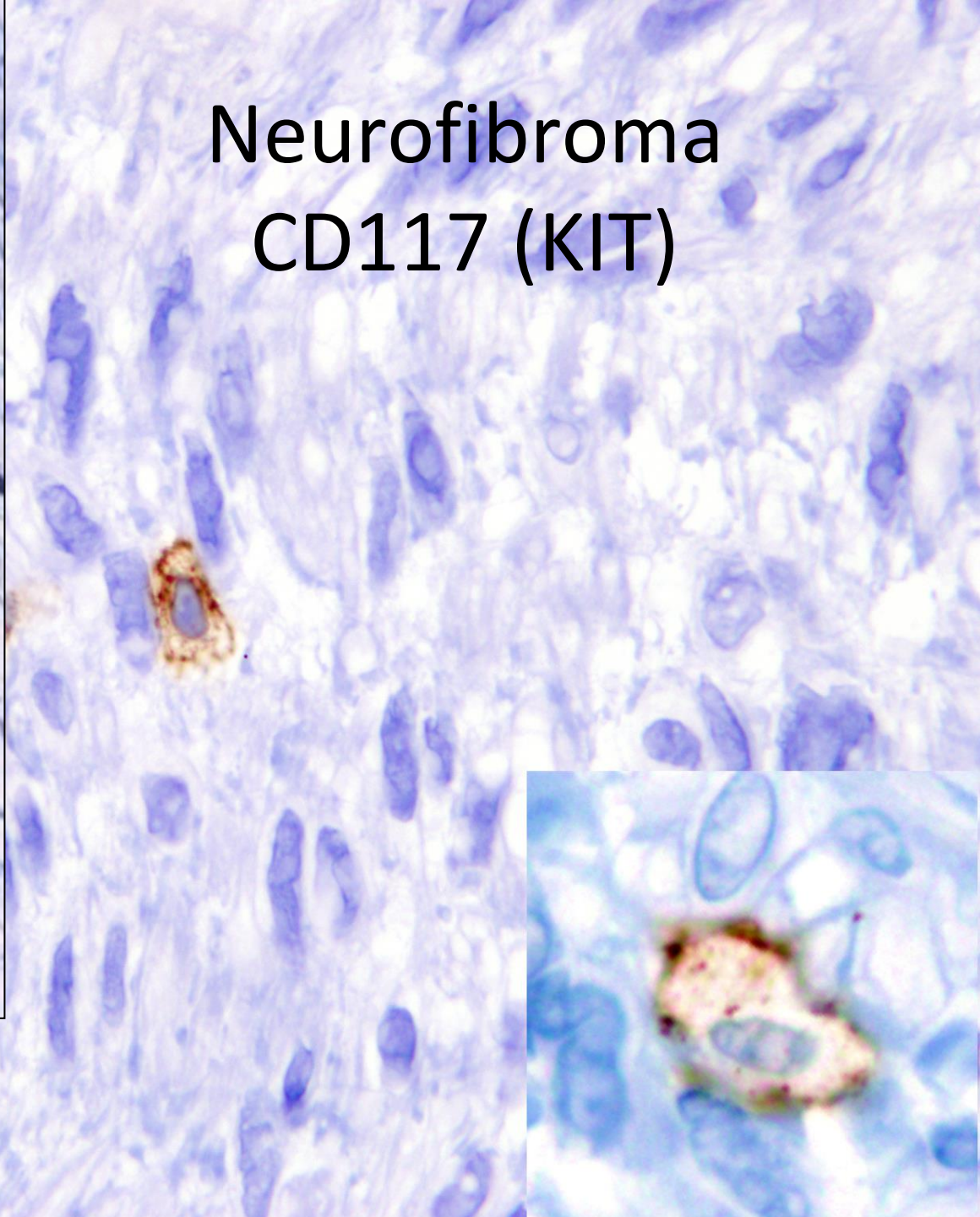
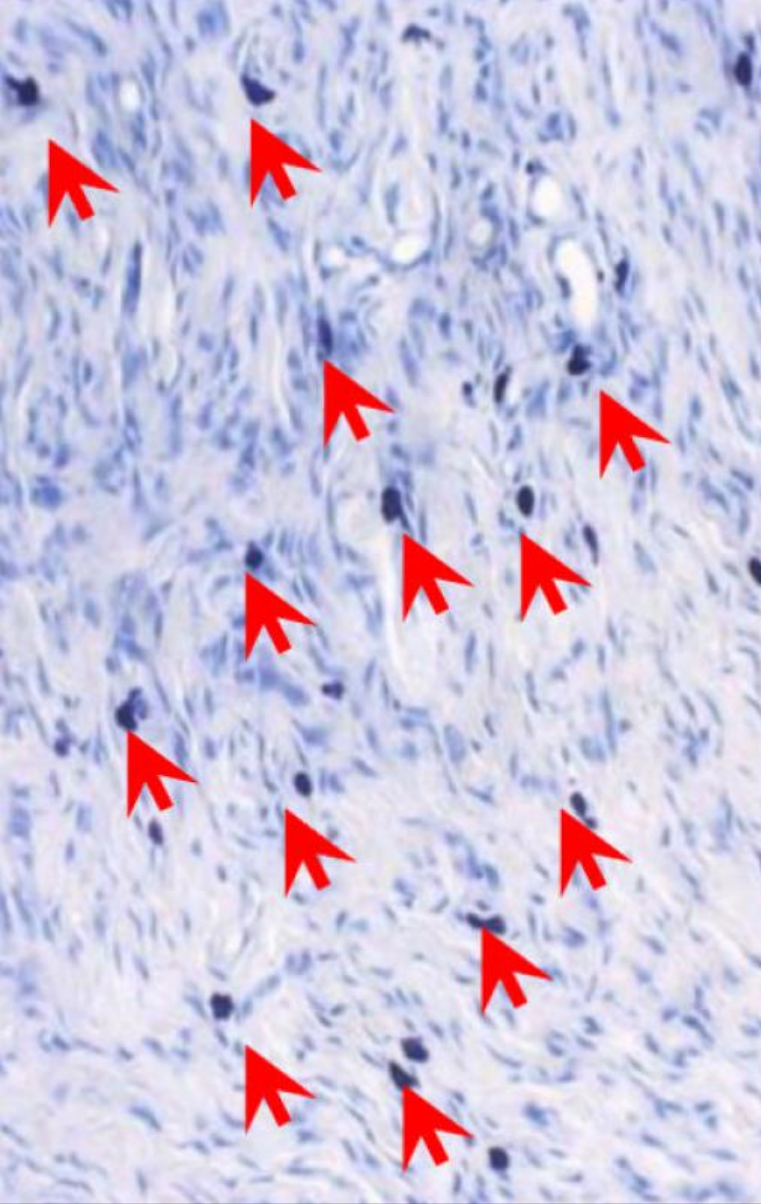
Neurofibroma



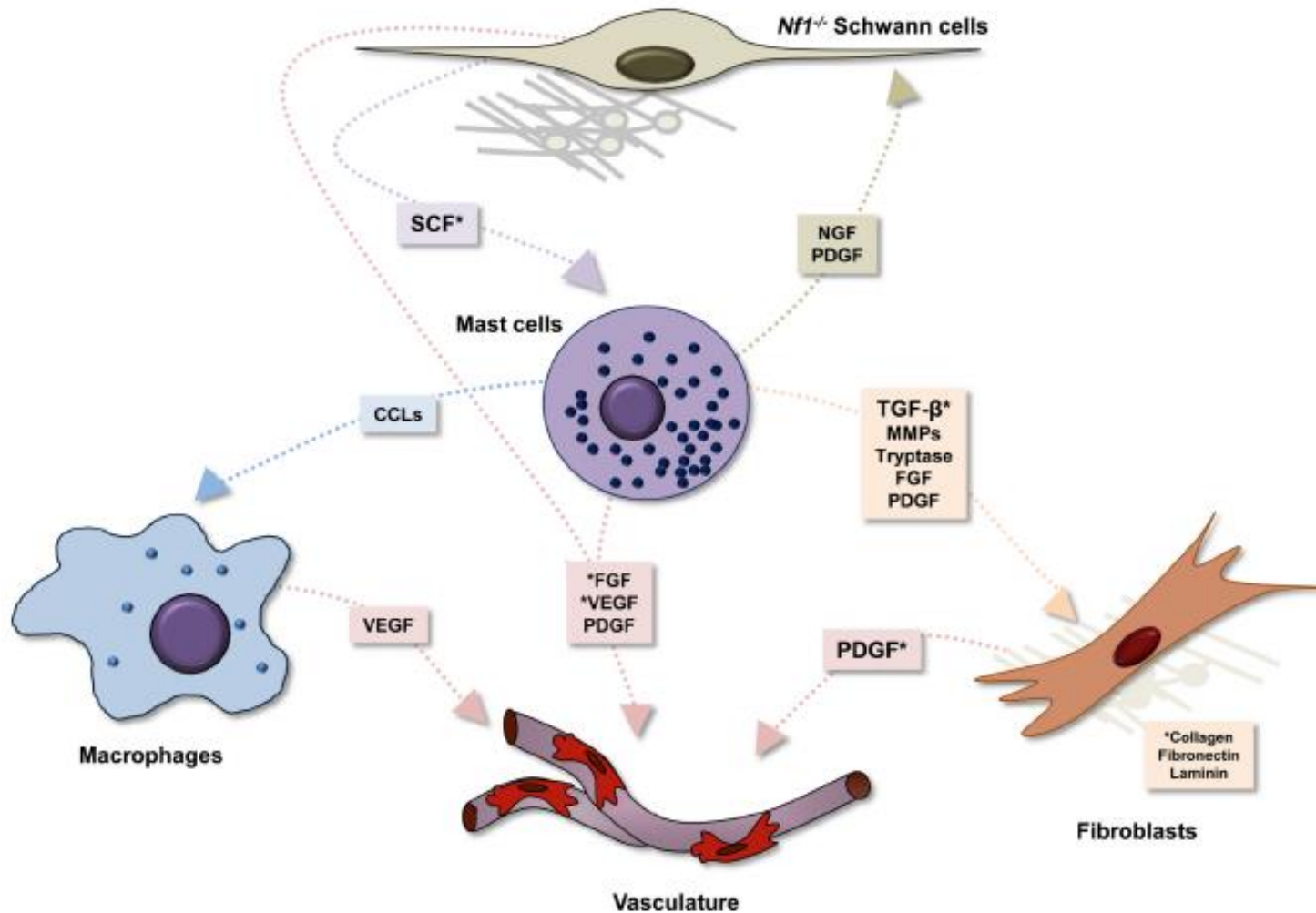
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Neurofibroma

CD117 (KIT)

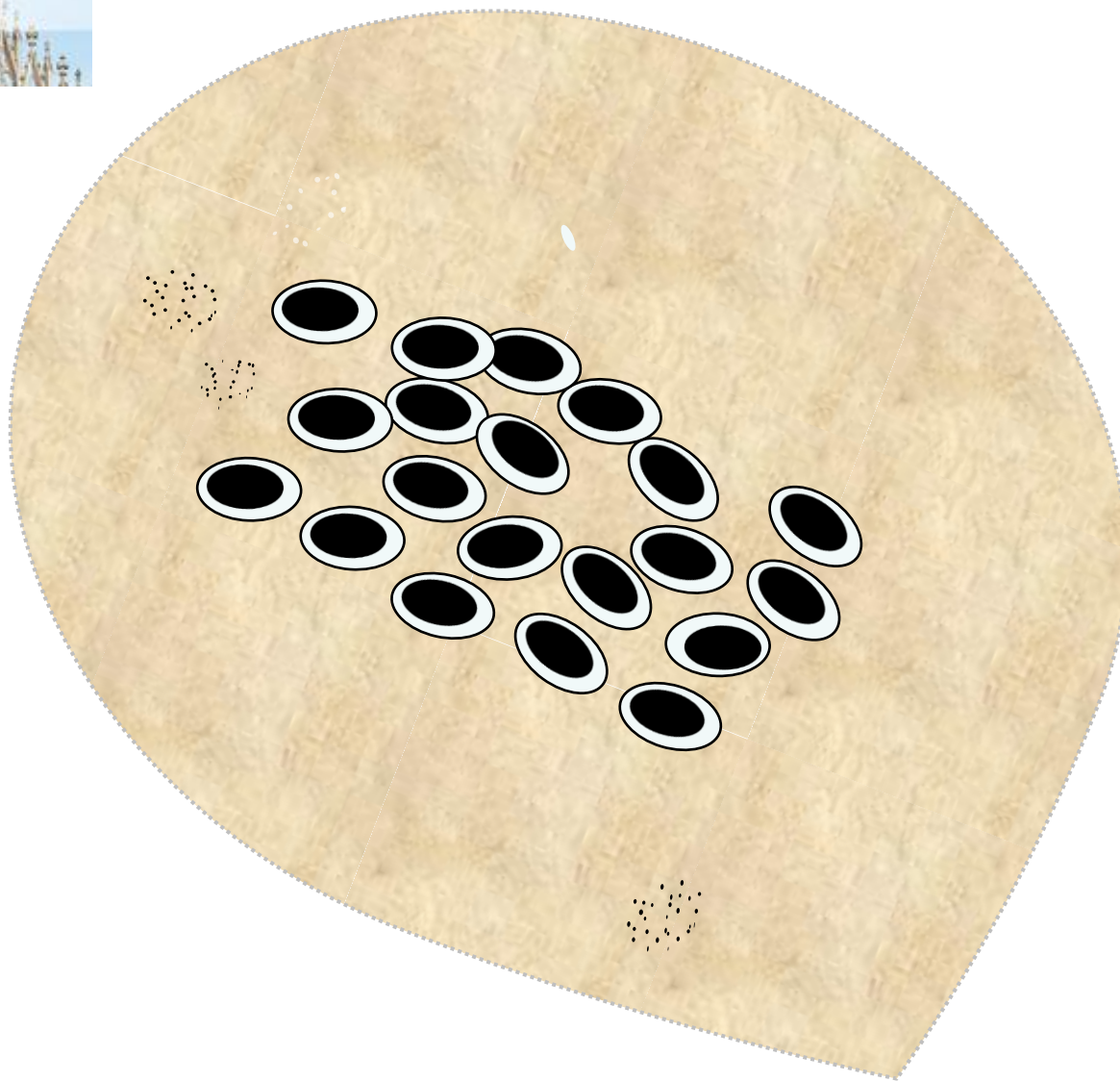


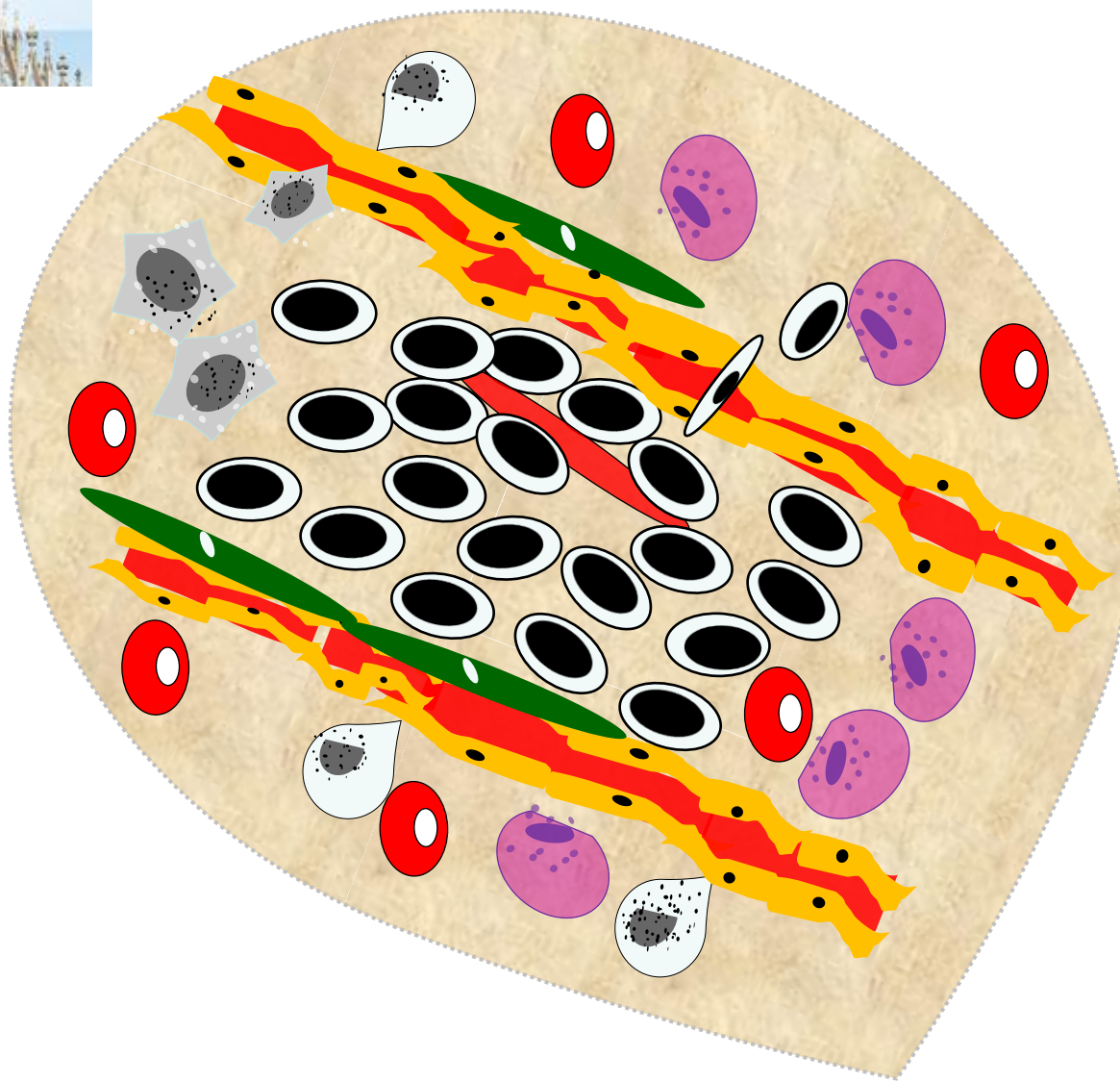
Tumor/stromal interactions in neurofibroma microenvironment

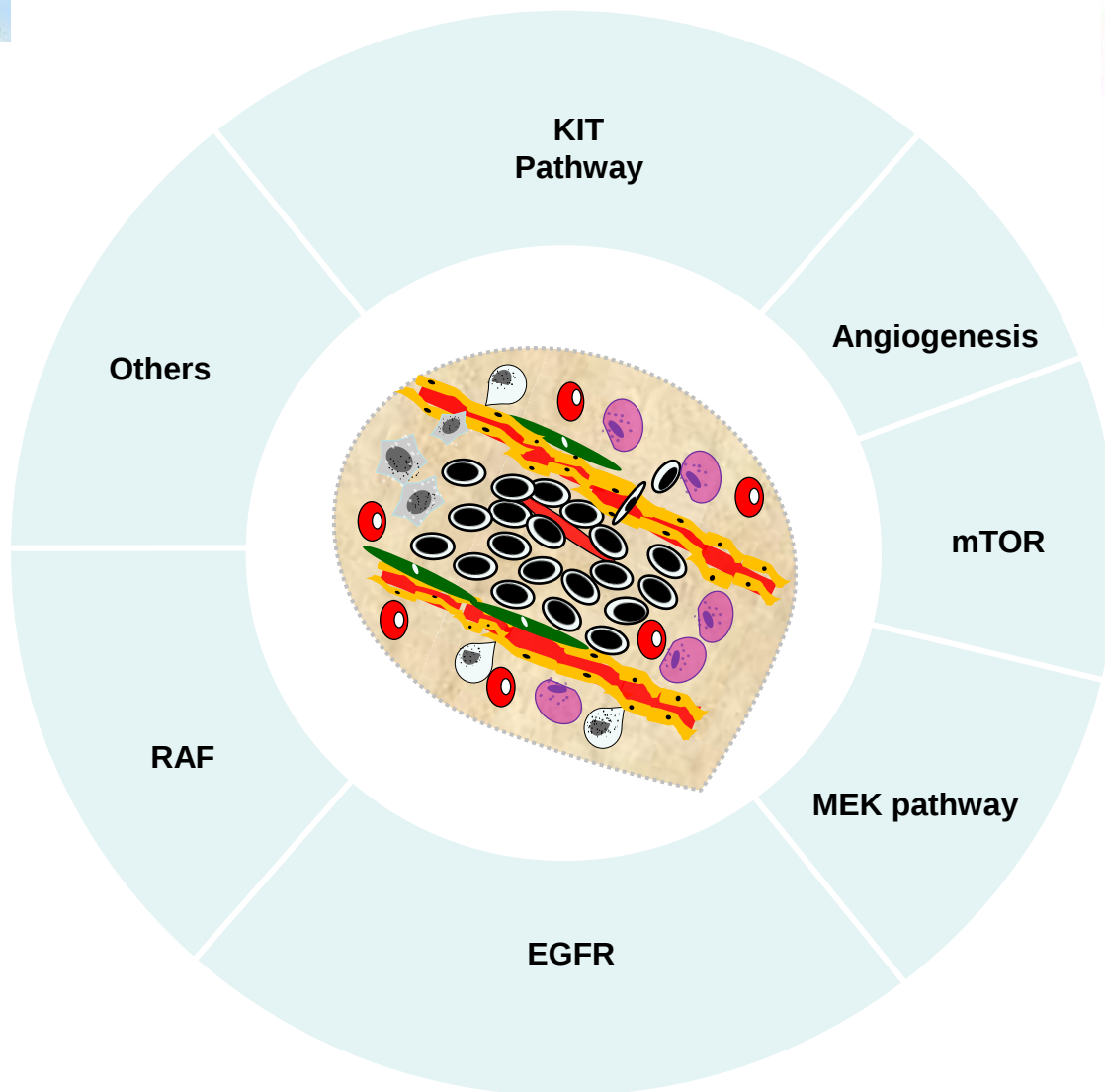




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HDAC I
HSP90
Survivin
WNT pathway
AURKA

Nilotinib

Imatinib

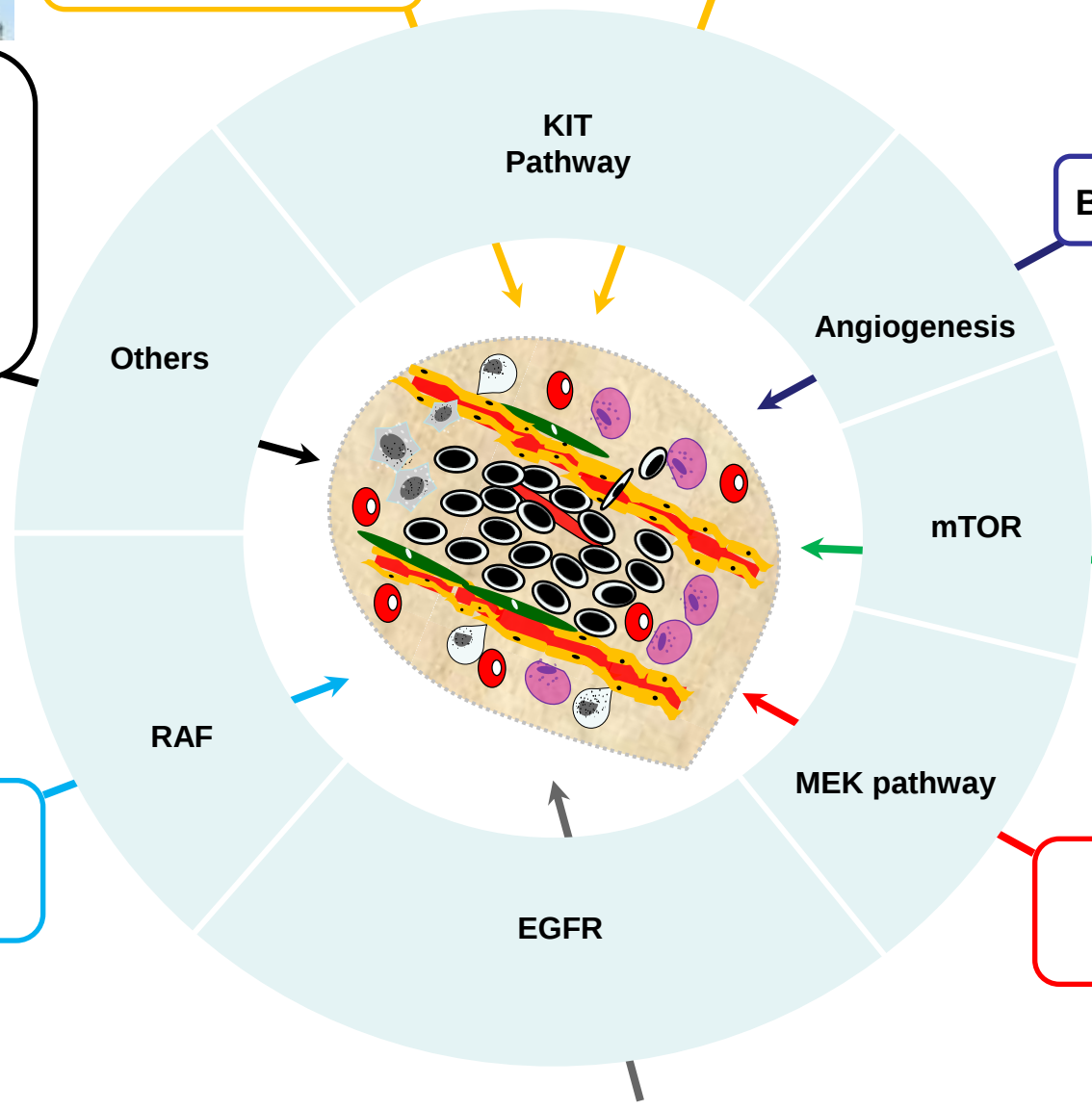
Bevacizumab

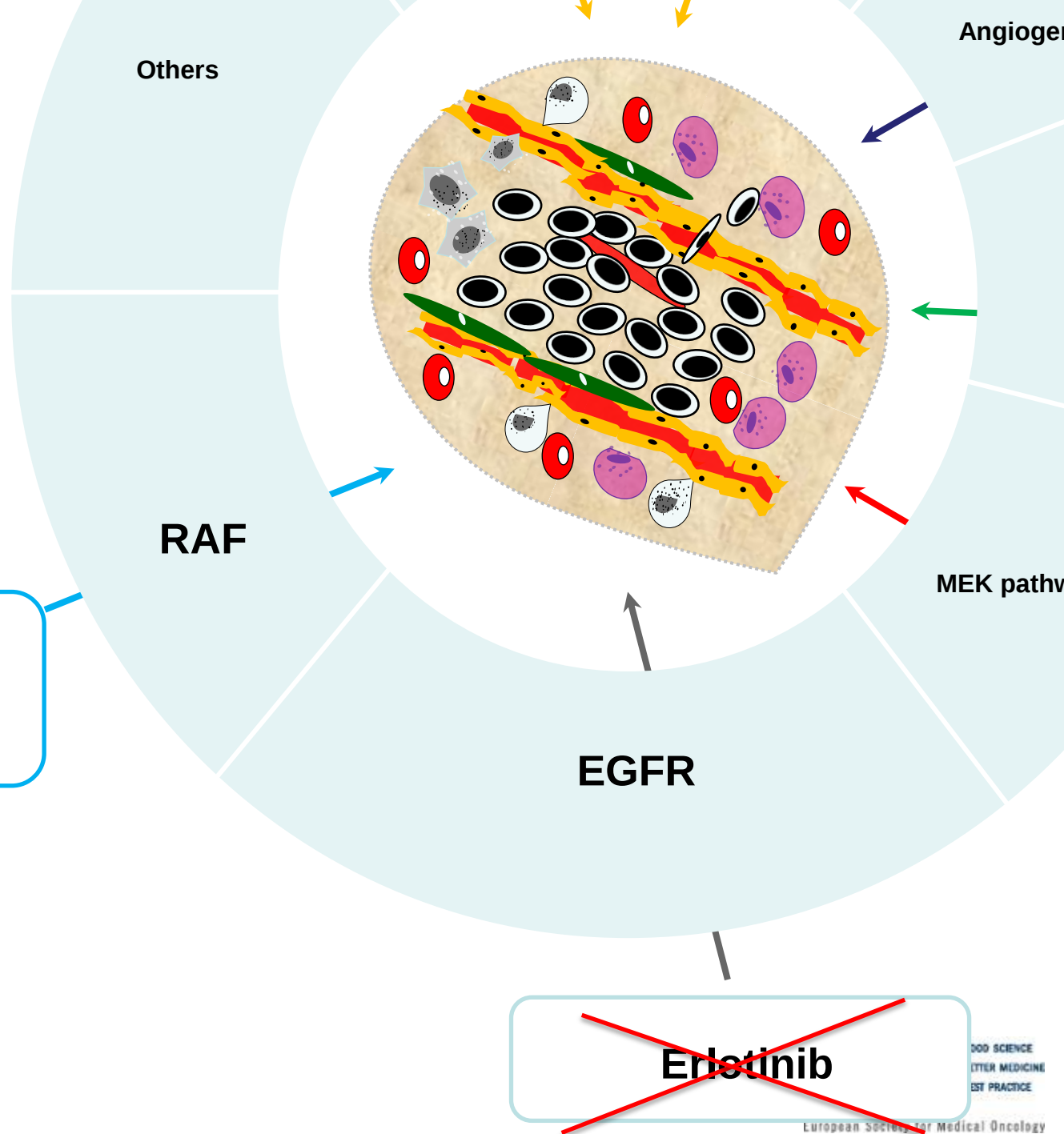
Everolimus

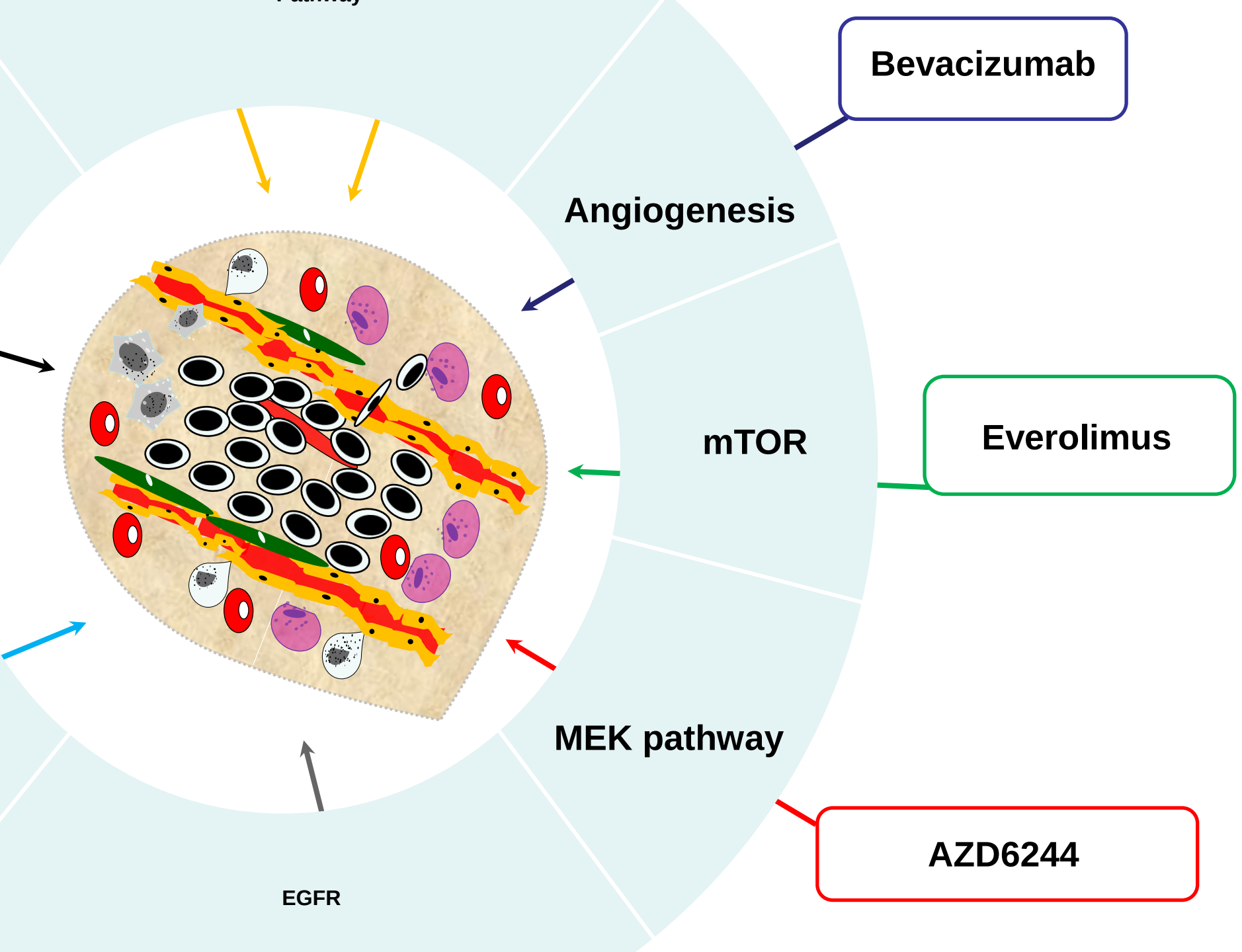
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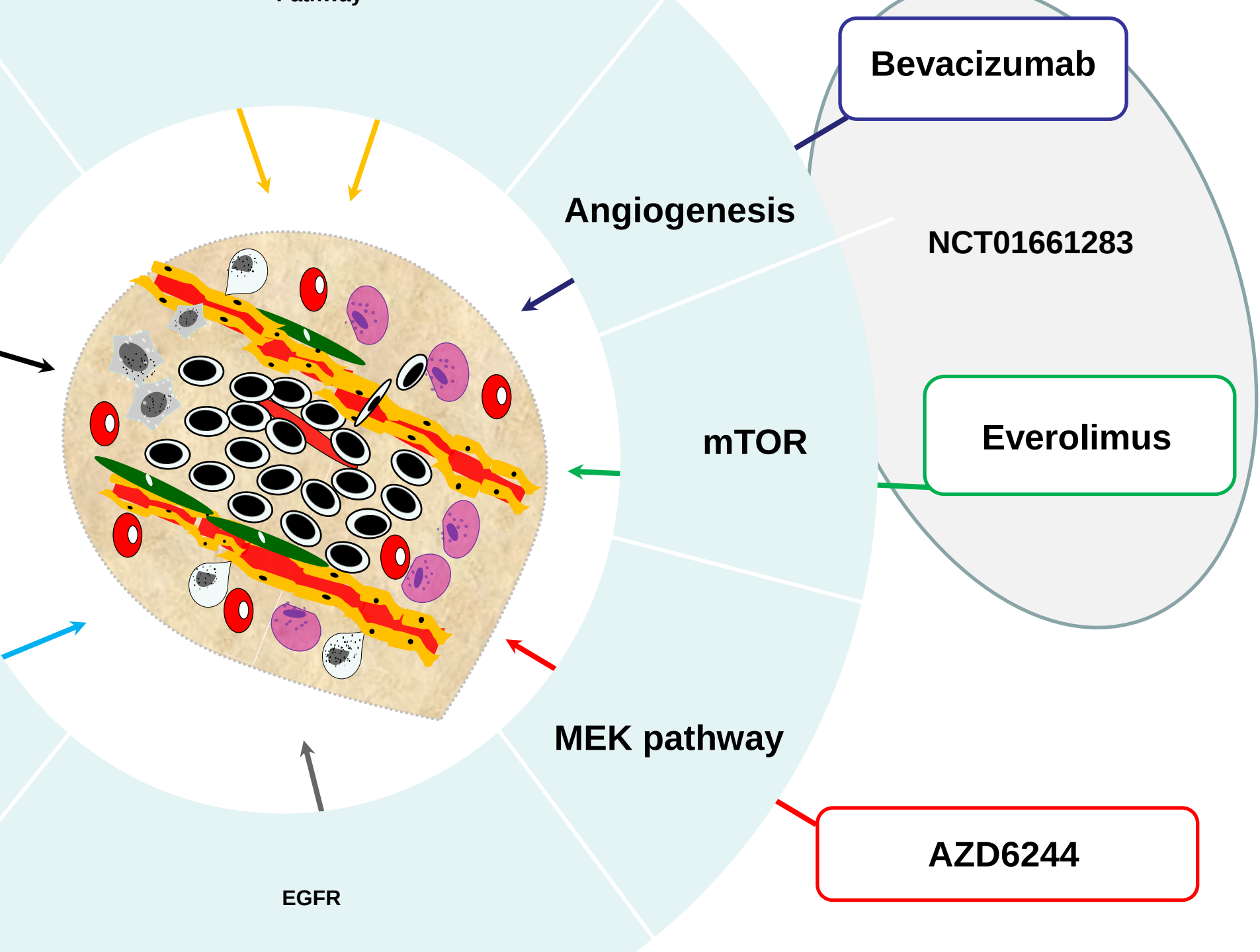
Erlotinib

Sorafenib

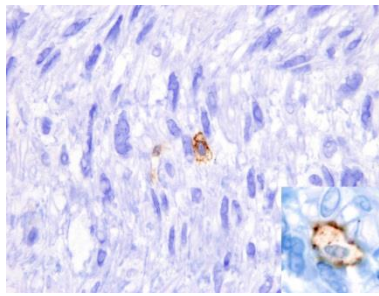






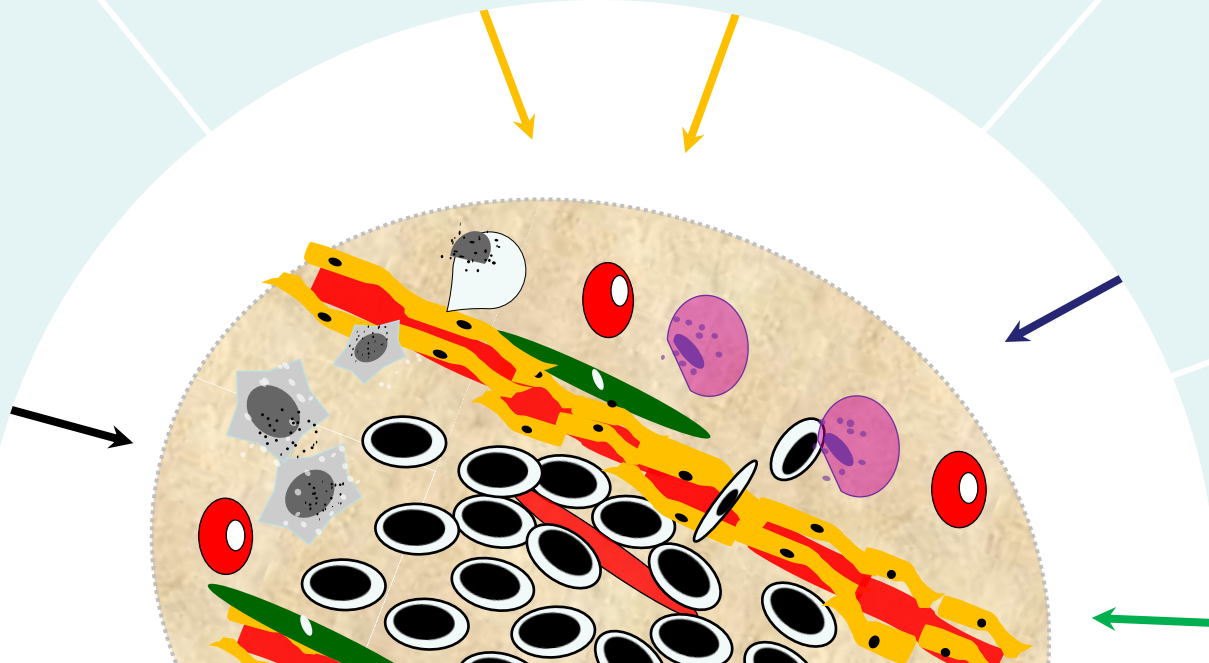


Nilotinib



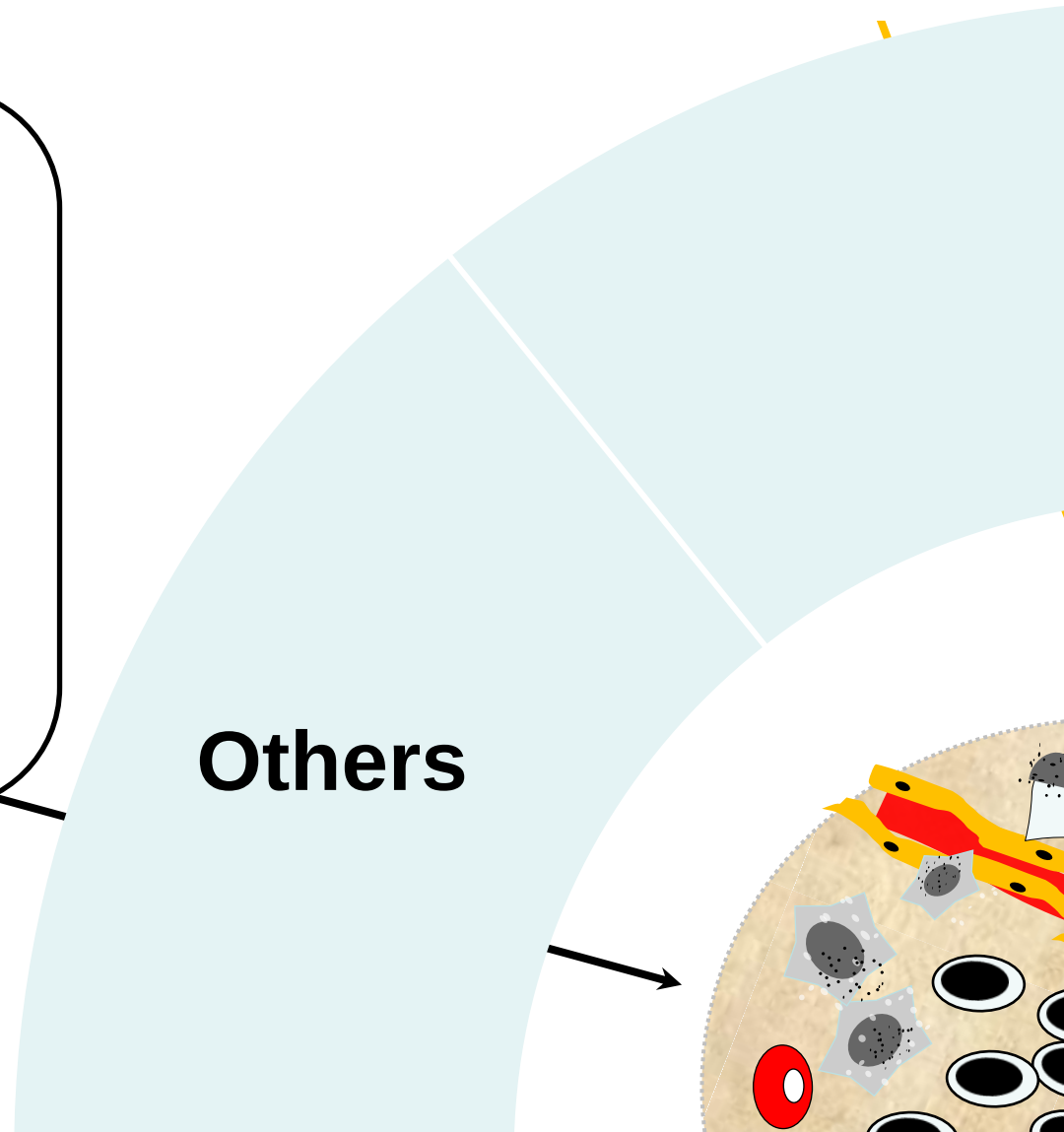
Imatinib

**KIT
Pathway**



HDAC i
HSP90
Survivin
WNT pathway
AURKA

Others



Challenges

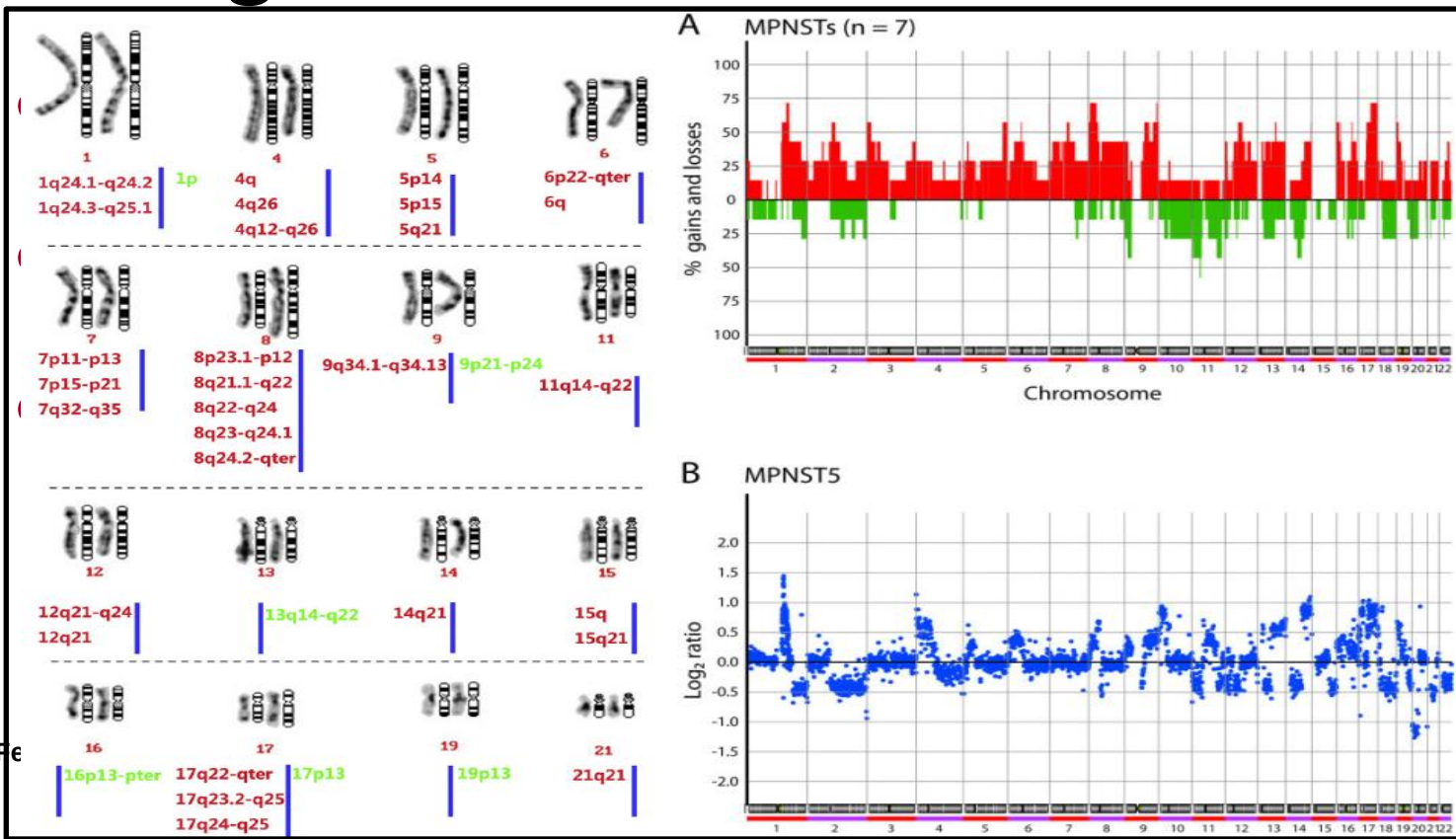
- Tumor heterogeneity (inter/intra)



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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

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NF1 mutations are common

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