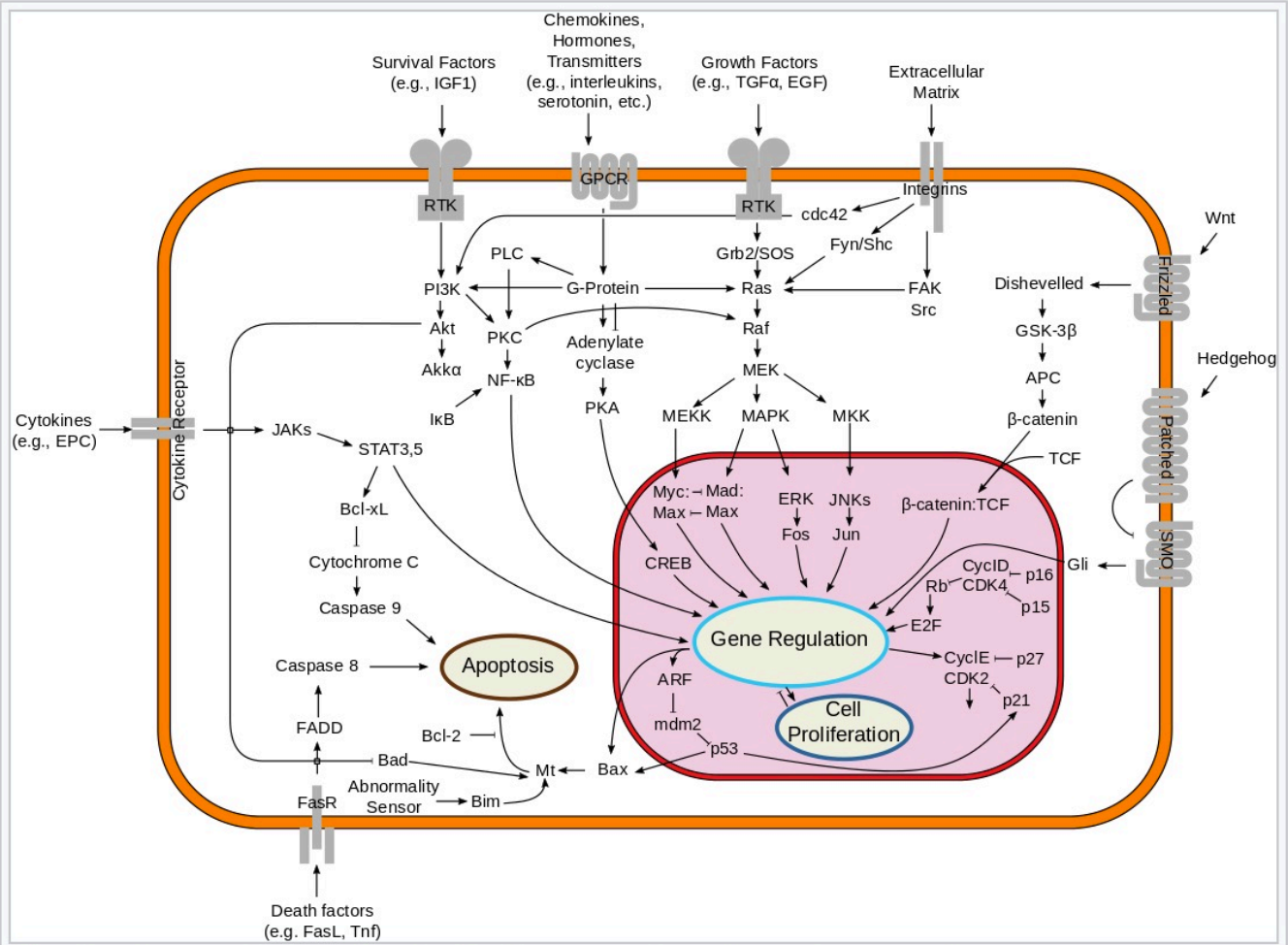
Smoothened (SMO)

In the absence of Hh, a cell-surface transmembrane protein called Patched (PTCH) acts to prevent high expression and activity of a 7 membrane spanning receptor called Smoothened (SMO).



Simplified representation of major signal transduction pathways in mammals.

A subset of meningiomas lacking NF2 alterations harbored recurrent oncogenic mutations in AKT1 (p.Glu17Lys) and SMO (p.Trp535Leu) and exhibited immunohistochemical evidence of activation of these pathways. These mutations were present in therapeutically challenging tumors of the skull base and higher grade. These results begin to define the spectrum of genetic alterations in meningiomas and identify potential therapeutic targets [1].

Identification of SMO and AKT1 mutations in meningiomas has raised the hope for targeted therapies. It would be useful to know the precise frequency of these mutations in anatomical subgroups and clarify their prognostic value.

Molecular diagnosis of SMO L412F/W535L and AKT1 E17K mutations improves prognostic evaluation in olfactory groove meningiomas and opens new therapeutic perspectives with SMO or AKT inhibitors for recurrent cases [2].

1)

Brastianos PK, Horowitz PM, Santagata S, Jones RT, McKenna A, Getz G, Ligon KL, Palescandolo E, Van Hummelen P, Ducar MD, Raza A, Sunkavalli A, Macconaill LE, Stemmer-Rachamimov AO, Louis DN, Hahn WC, Dunn IF, Beroukhim R. Genomic sequencing of meningiomas identifies oncogenic SMO and AKT1 mutations. Nat Genet. 2013 Mar;45(3):285-9. doi: 10.1038/ng.2526. PubMed PMID: 23334667; PubMed Central PMCID: PMC3739288.

2)

Boetto J, Bielle F, Sanson M, Peyre M, Kalamarides M. SMO mutation status defines a distinct and frequent molecular subgroup in olfactory groove meningiomas. Neuro Oncol. 2017 Jan 12. pii: now276. doi: 10.1093/neuonc/now276. [Epub ahead of print] PubMed PMID: 28082415.