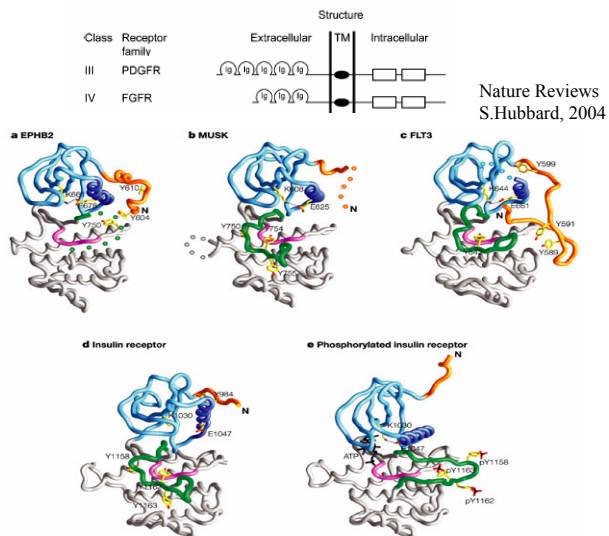


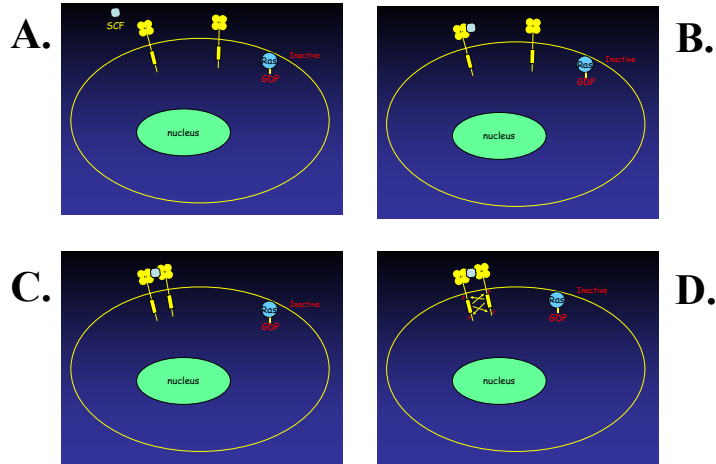
Autoinhibition of RTK

Amélie, Christina, Aina and Fabrice

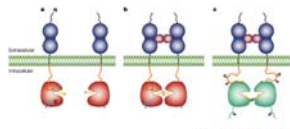
Receptor tyrosine kinase



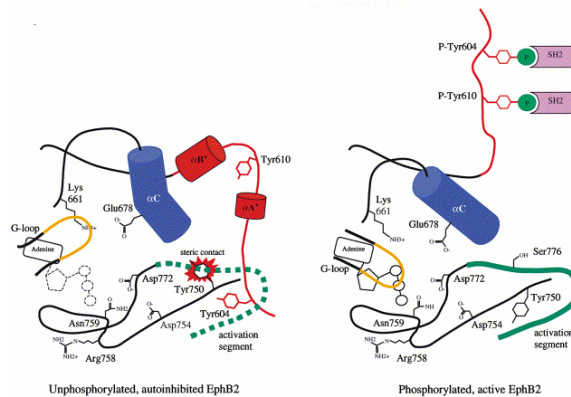
Receptor tyrosine kinase activation



Autoinhibition mechanism



Nature Reviews
S.Hubbard, 2004



, Wybenga-Groot,
Cell, 2001

Aims and approach

- To find sequences of different RTK using Pubmed, Blast
- Clustal alignments to find similarities between RTK sequences, or subgroups of RTKs
- To confirm autoinhibition with Scansite to find affinity for substrates
- Find structures to illustrate autoinhibition and activation states

Alignments

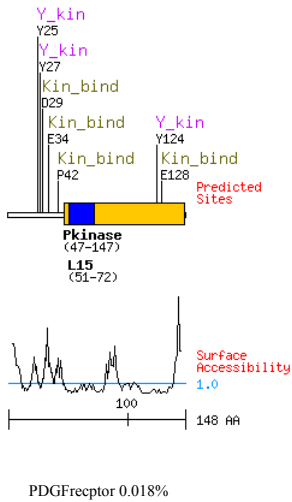
```
5c-kit      AYKYLQKPMYEVQWKVVEEINGNNYVVIDPTQLPVDHKNVFFRNRLSPGKTLGAGAFQKV
7FLT3      KYKKQFRYESQLQMVQVTGSSDNEYFVDFREYEDLKNVFFRENLEFGKVLGSGAFQKV
6PDGFRbeta ---RKPRYEIRWKVIESVSSDGHEYIIVDPVQLPVDSTNELFRDQLVLGRTLGSAGFQV

1EPHB2     RRGFERADSEYTDKLGHYTSGHMTPGMKIIVDPFTVEDPNEAVREFAKEIDISCVKIEQV
2EphA4     ----RRSKYSKAKQEADEEKHLNQGVRTIVDPFTVEDPNQAVREFAKEIDASCIKIEKV

8IHR       RKRQPDGGLPLYASSNPEVLSASDVFPQSVVVDENEVSREKITLLRELGGQSGFMVYE
```

■ Tyrosine residues
■ Tyrosine kinase domain

Substrate affinity

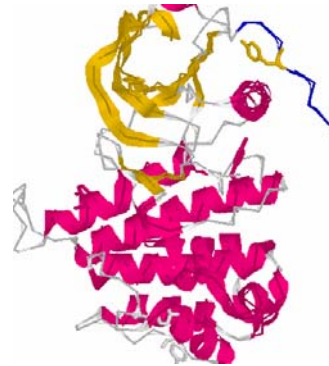


Tyrosine kinase group (Y _{kin})			
PDGFR Kin		Gene Card PDGFRB	
Site	Score	Percentile	Sequence
Y25	0.2611	0.018 %	TGSSDNEYFYVDFRE 1.046
EGFR Kinase		Gene Card EGFR	
Site	Score	Percentile	Sequence
Y25	0.2943	0.022 %	TGSSDNEYFYVDFRE 1.046
PDGFR Kin		Gene Card PDGFRB	
Site	Score	Percentile	Sequence
Y27	0.3319	0.147 %	SSDNEYFYVDFREYE 0.523
Fgr Kinase		Gene Card FGR	
Site	Score	Percentile	Sequence
Y25	0.3909	0.261 %	TGSSDNEYFYVDFRE 1.046
EGFR Kinase		Gene Card EGFR	
Site	Score	Percentile	Sequence
Y124	0.4007	0.391 %	CTLSGPIYLIFEYCC 0.195
Itk Kinase		Gene Card ITK	
Site	Score	Percentile	Sequence
Y124	0.4218	0.547 %	CTLSGPIYLIFEYCC 0.195
Itk Kinase		Gene Card ITK	
Site	Score	Percentile	Sequence
Y27	0.4219	0.548 %	SSDNEYFYVDFREYE 0.523

Structure models



Inactive(insulin receptor)



Active(FLT3 receptor)

