Aberrations of Signal Transduction in Cancers

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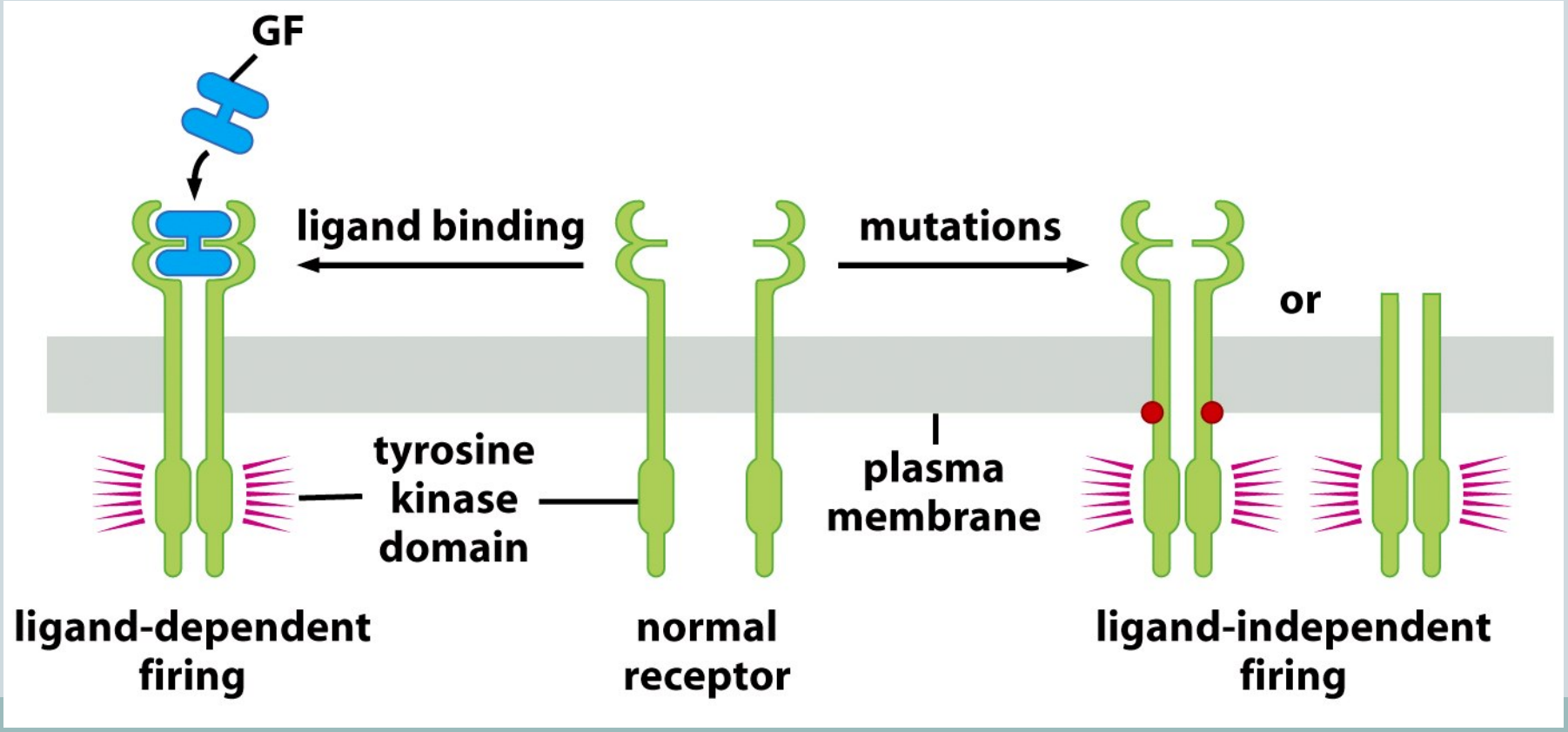
"All decisions made by an individual cell about its proliferation must, by necessity, represent a consensus decision shared with the cells that reside in its neighborhood"

Growth Factors and Their Receptors

- EGF, TGF-α, PDGF, VEGF etc
- Termed as **mitogens** – ability to induce cell proliferation
- Growth factors are essential for cell survival – cells in culture require serum (which contains a variety of growth factors)
- Growth factors require cell surface receptors for action

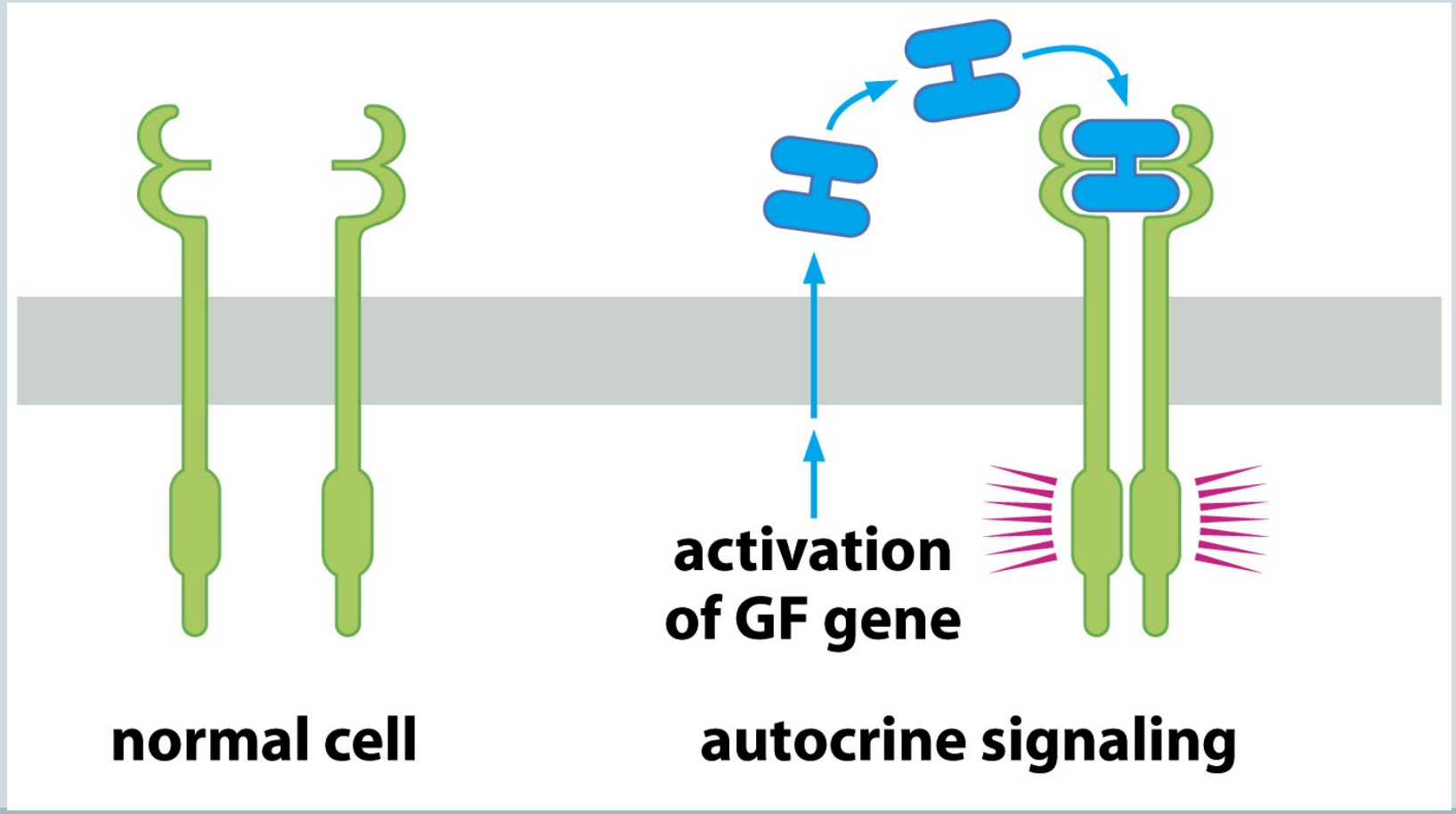
How Receptor Function Becomes Deregulated

- Loss of regulatory domains
- Constitutive dimerization due to gene fusion



How Receptor Function Becomes Deregulated

- Autocrine signaling

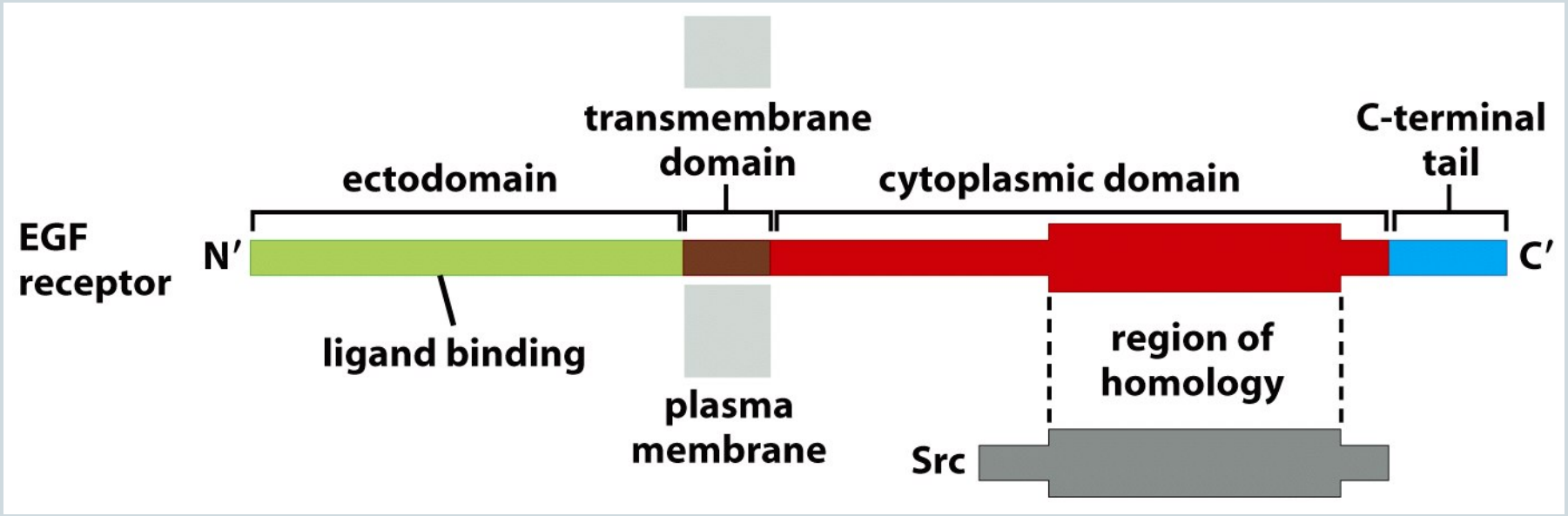


Src Protein as a Tyrosine Kinase

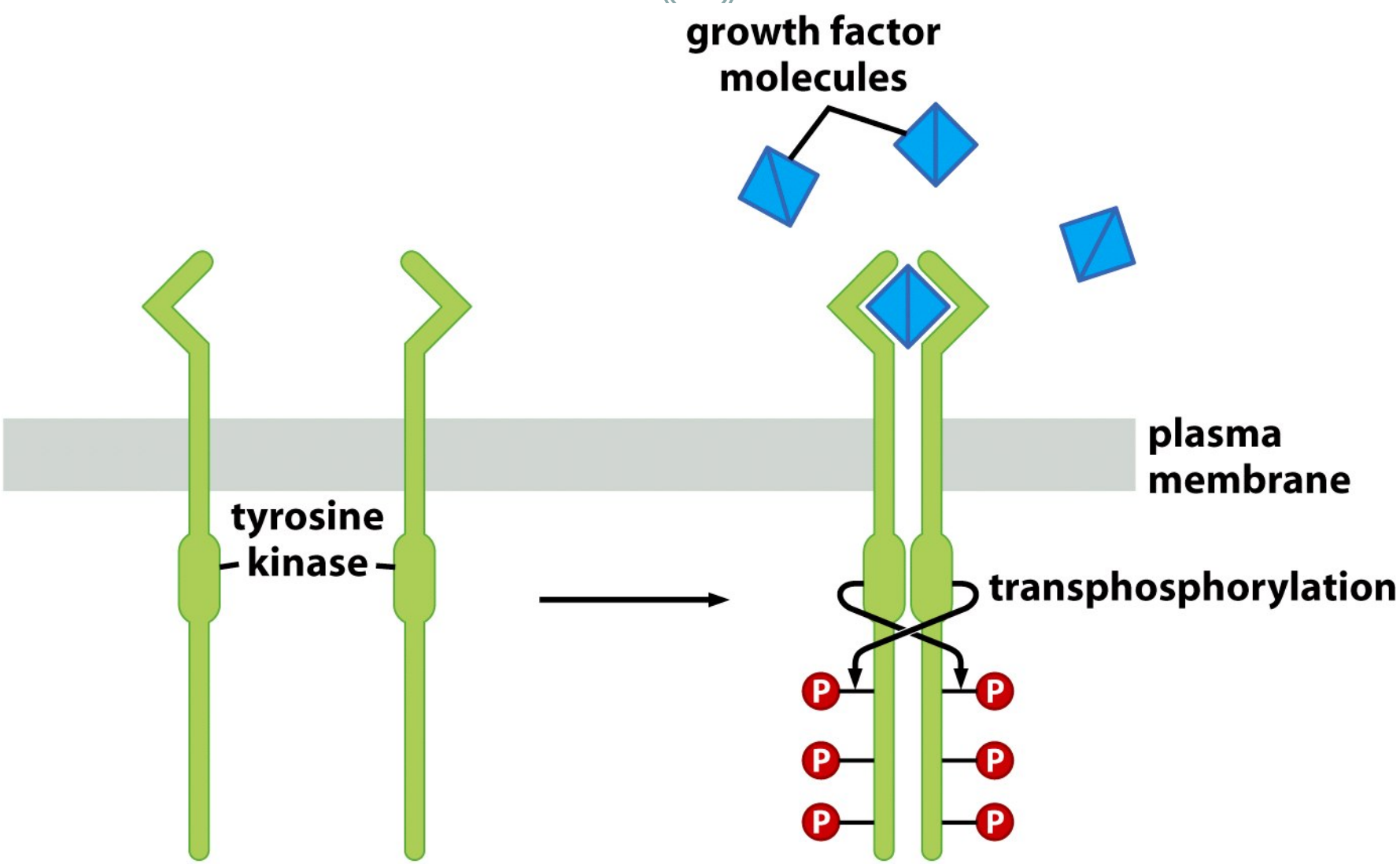
- Src – first cellular oncoprotein to be studied
- Most kinases found till then were Serine and Threonine kinases – more than 99% of the phosphoamino acids in normal cells are phosphothronine and phosphoserine
- Src – Tyrosine kinase; phosphotyrosine constitutes only 0.05 – 0.1 % of total phosphoamino acids → but very important!

EGFR: Also a Tyrosine Kinase

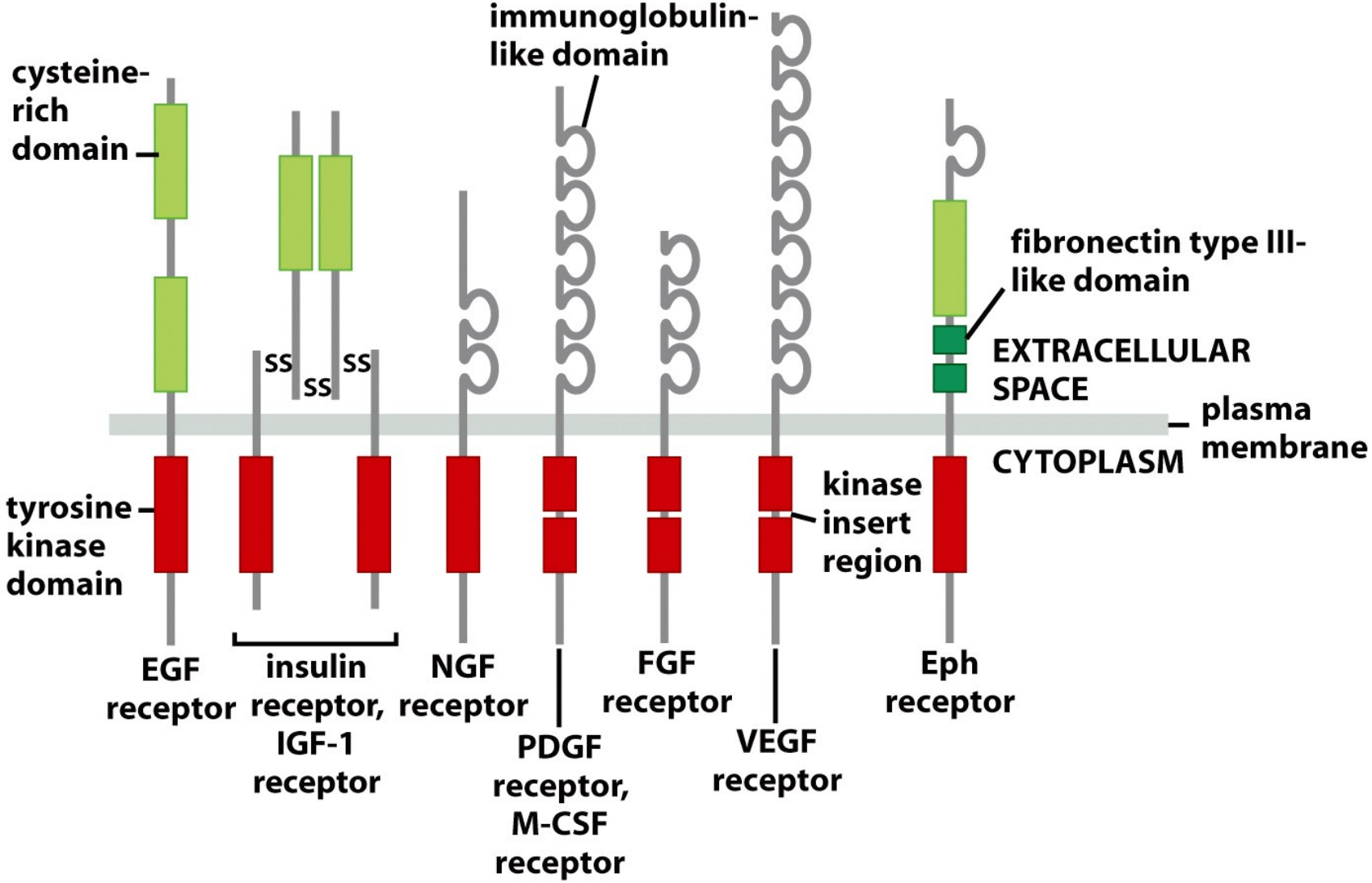
- 3 main domains – Ecto, transmembrane, cytoplasmic
- Cytoplasmic domain – homologous to Src



EGFR Forms Heterodimers Which Transphosphorylate Each Other



Other Tyrosine Kinase Receptors



Integrins and the Extracellular Matrix

- Normal cells require attachment to a solid substrate to proliferate → **Anchorage dependence**
- In the absence of attachment, normal cells undergo a form of programmed cell death, termed **Anoikis**
- Cells "sense" whether they are in contact with other cells or to a substrate through cell surface receptors – **Integrins**
- Signals transduced by integrins → ultimately affect **cell shape and motility**

Further Reading

- **The Biology of Cancer**, R. A. Weinberg