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OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

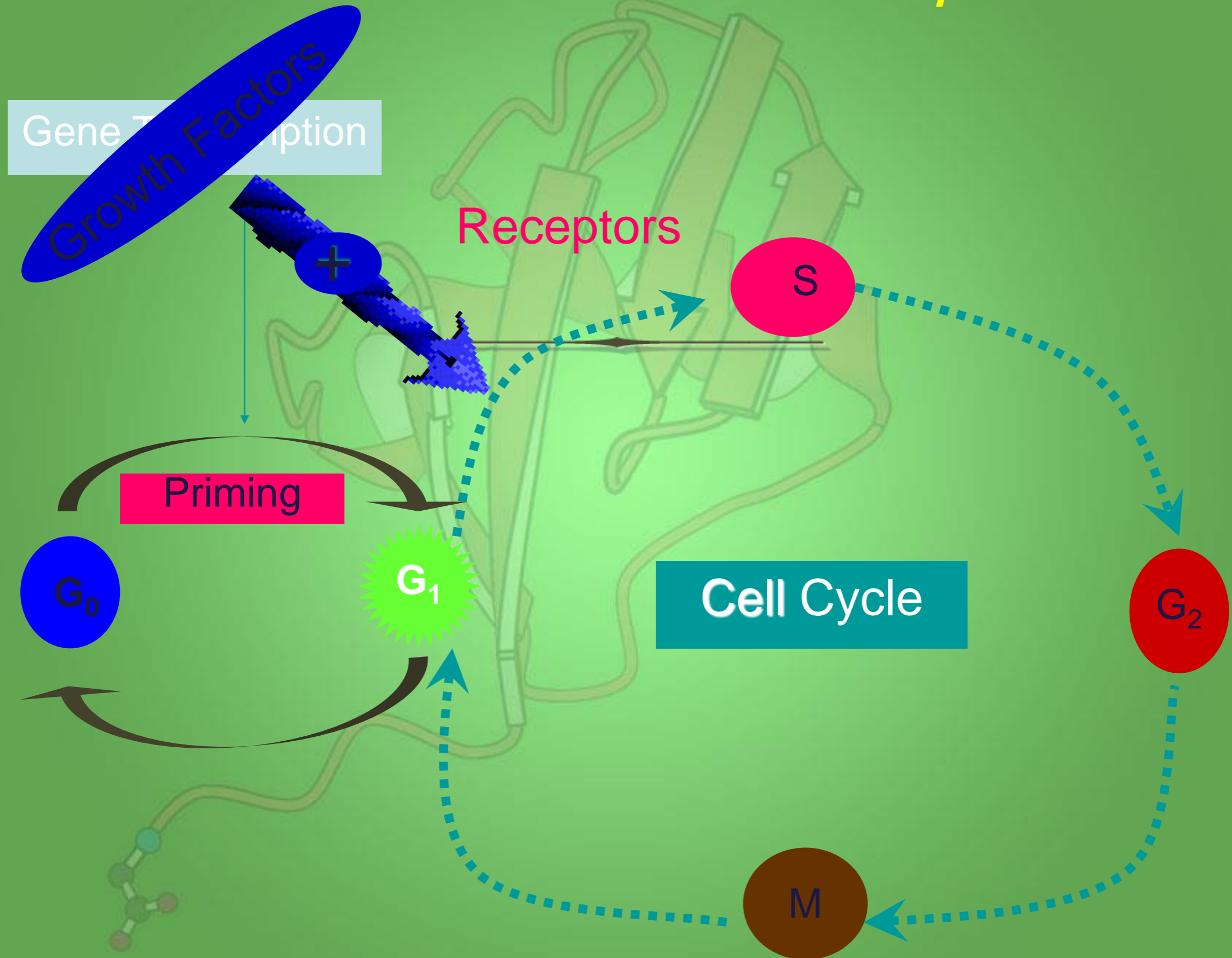
OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

CELLULAR AND MOLECULAR ACTIONS OF GROWTH FACTORS

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Growth Factors & Cell Cycle



- Growth factors and their receptors are important signaling molecules, which are involved in the regulation of cell growth.
- Epidermal growth factor (EGF) pathway plays an important role in tumorigenesis, including Hepatocellular Carcinoma. EGF polymorphisms are associated with susceptibility to several types of cancers.
- Epidermal growth factor receptor (EGFR) is considered as an important signaling hub where different proliferative and survival signals converge.

- Overexpression/activation of EGFR is associated with metastasis, poor prognosis and resistance to chemotherapy.
- EGFR is overexpressed or activated by autocrine or paracrine growth factor loops in at least 50% of epithelial malignancies.

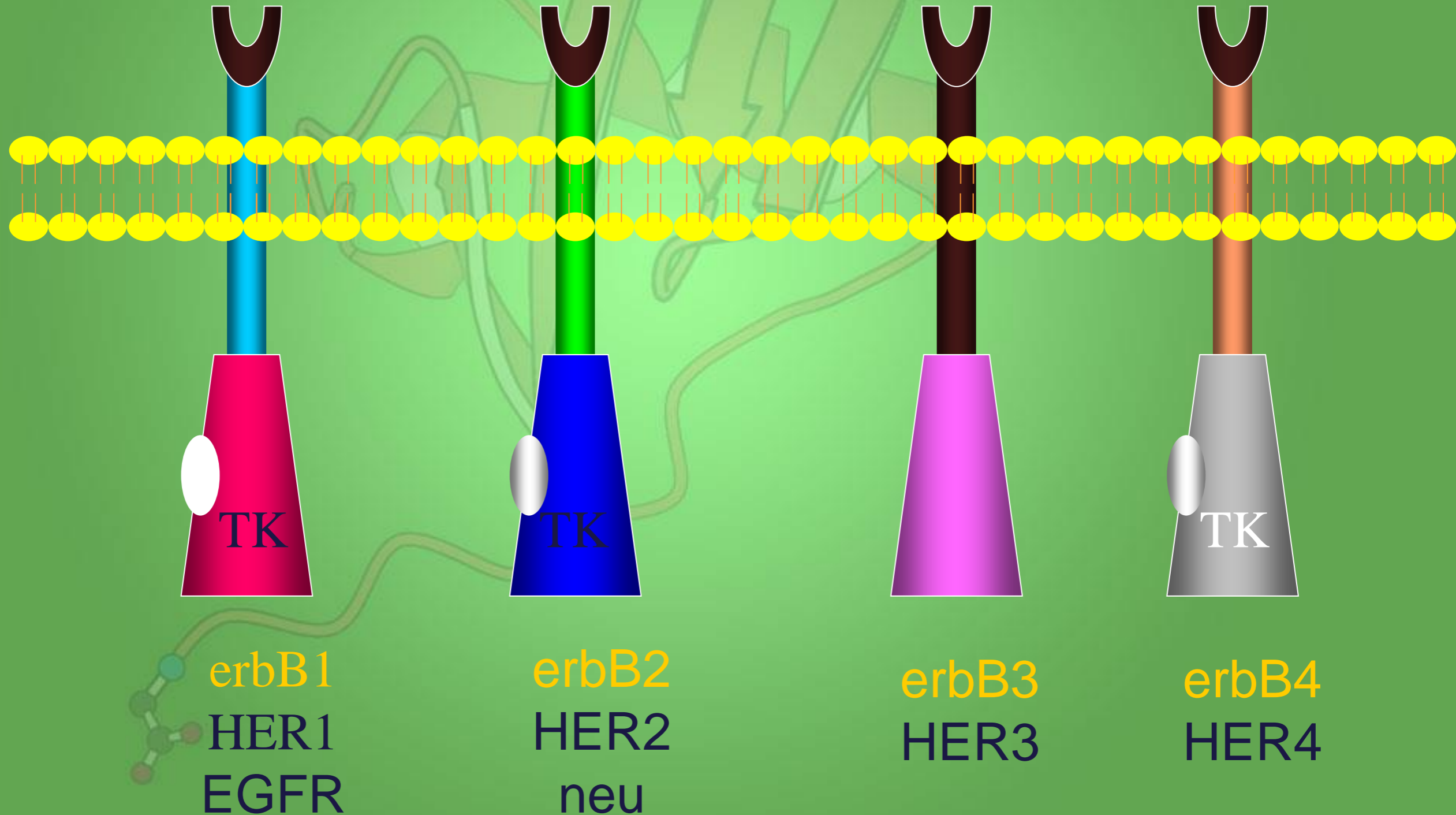
Human Epidermal Growth Factor Receptor Family

EGF, TGF α , β Cellulin
Amphiregulin, HB-EGF

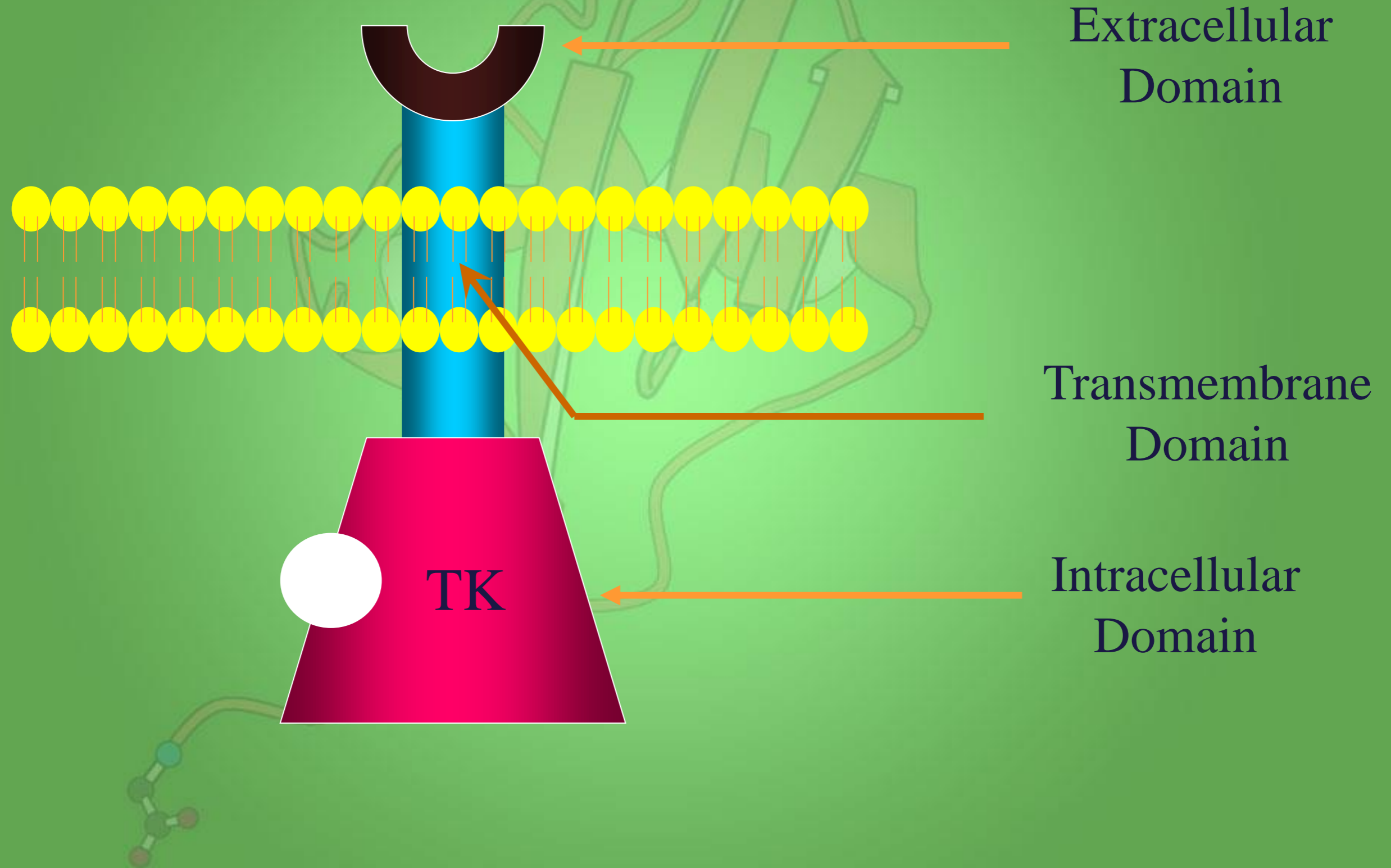
No specific ligands -
often acts as
dimer partner

Heregulins

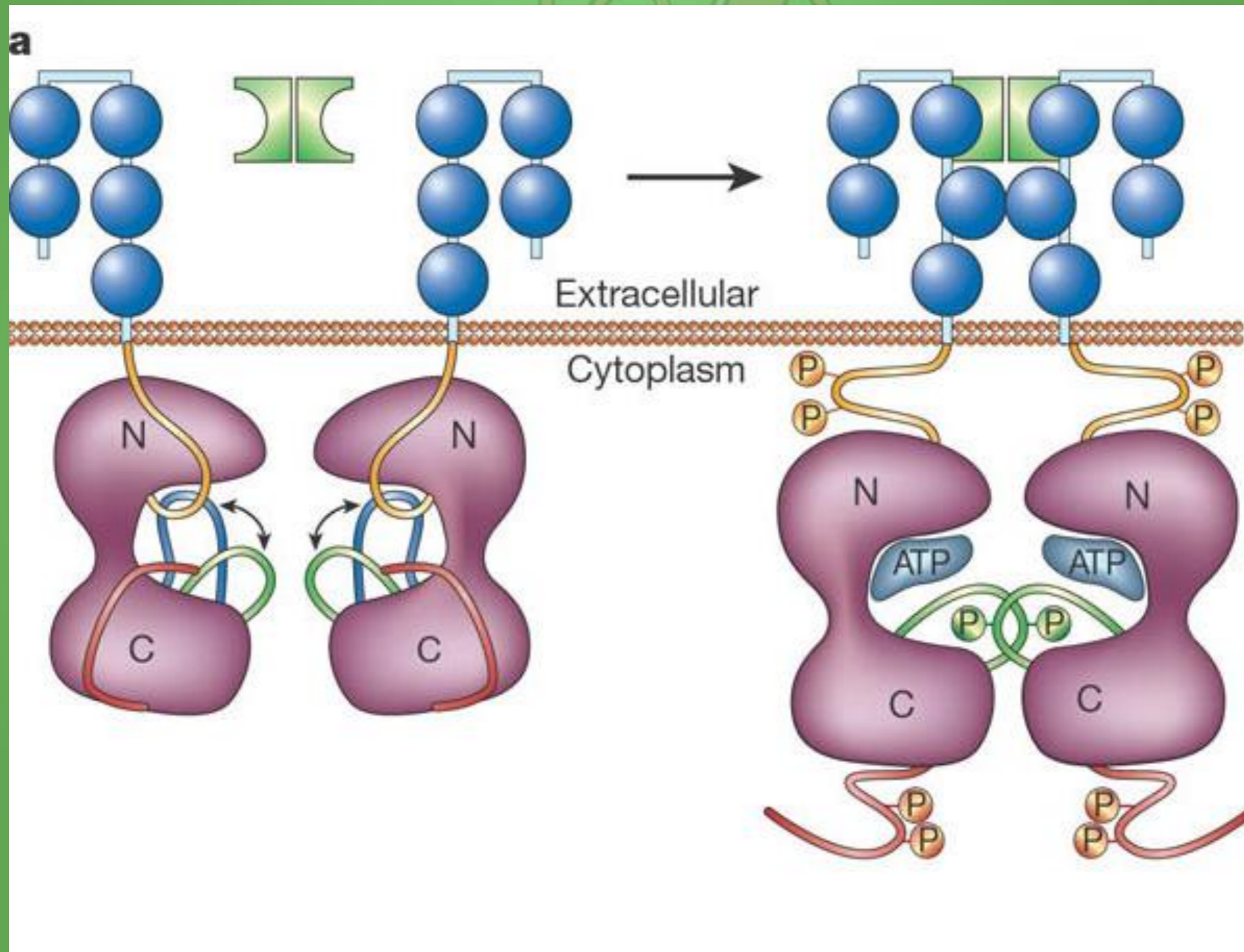
NRG2
NRG3
Heregulins
 β -cellulin



EGFR Structure

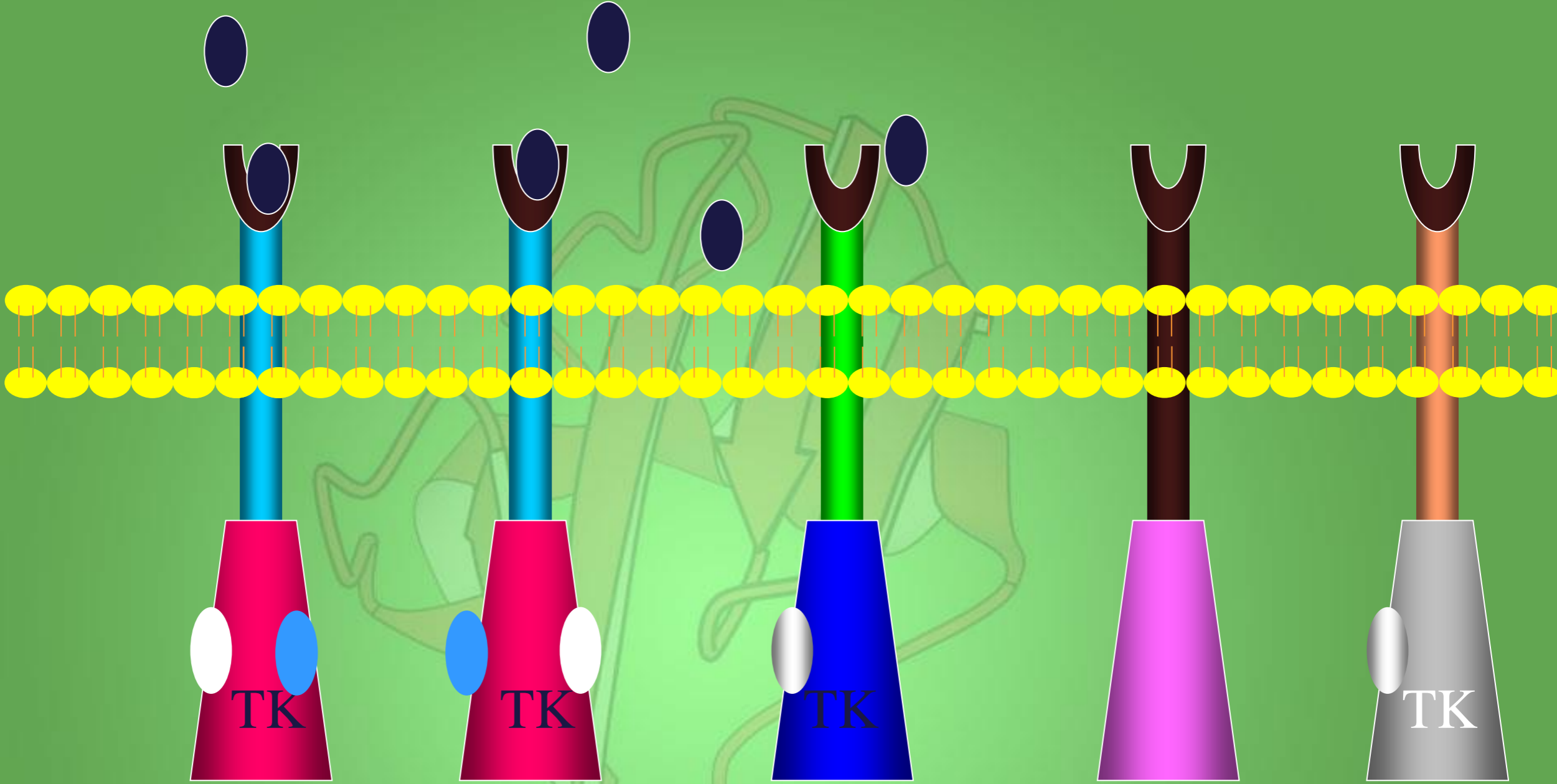


Receptor Dimerization and Kinase Activation



From Hunter (2001) Nature 411,355.

EGFR Stimulation & dimerisation



EGFR Homo Dimerisation

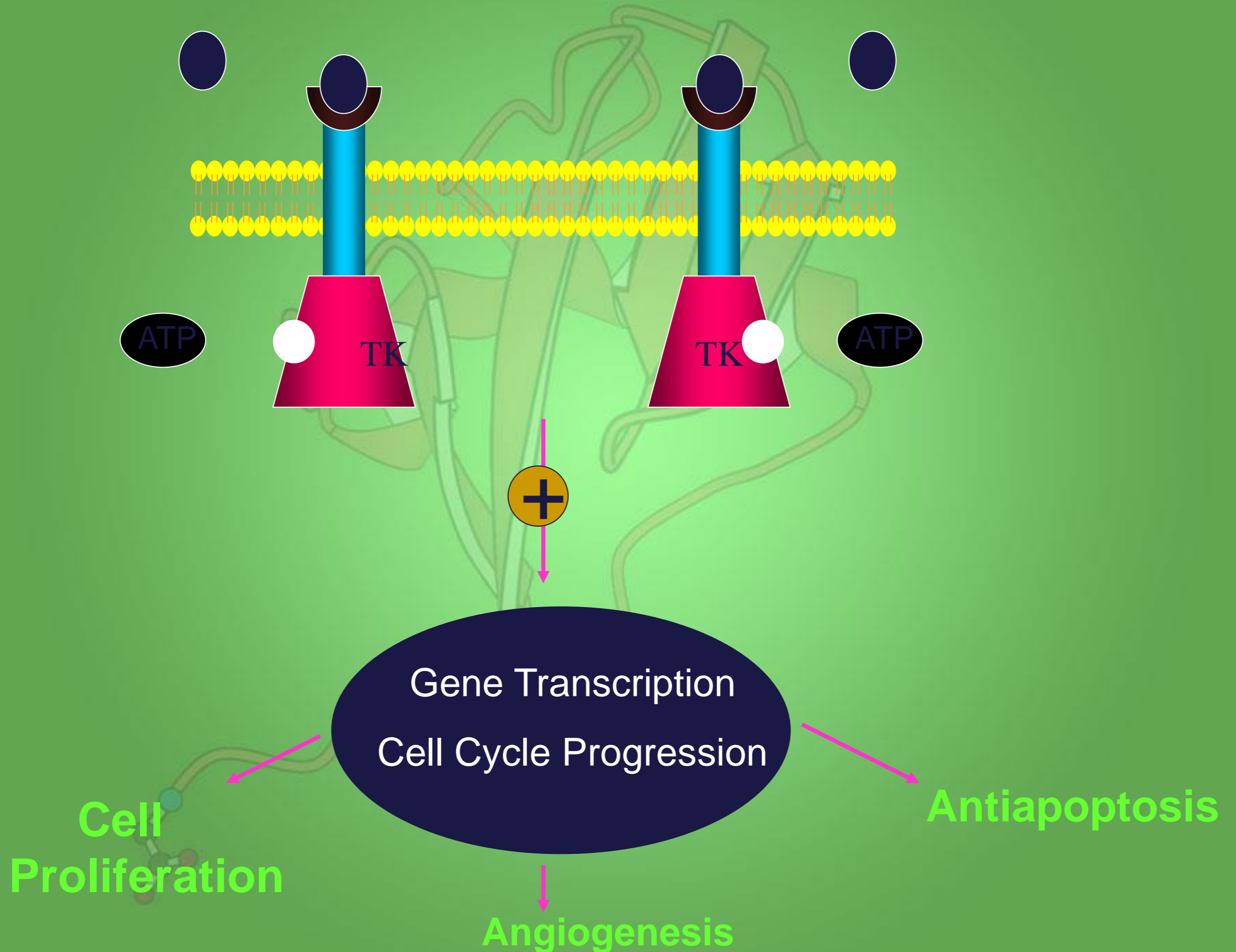
erbB1
HER1
EGFR

erbB2
HER2
neu

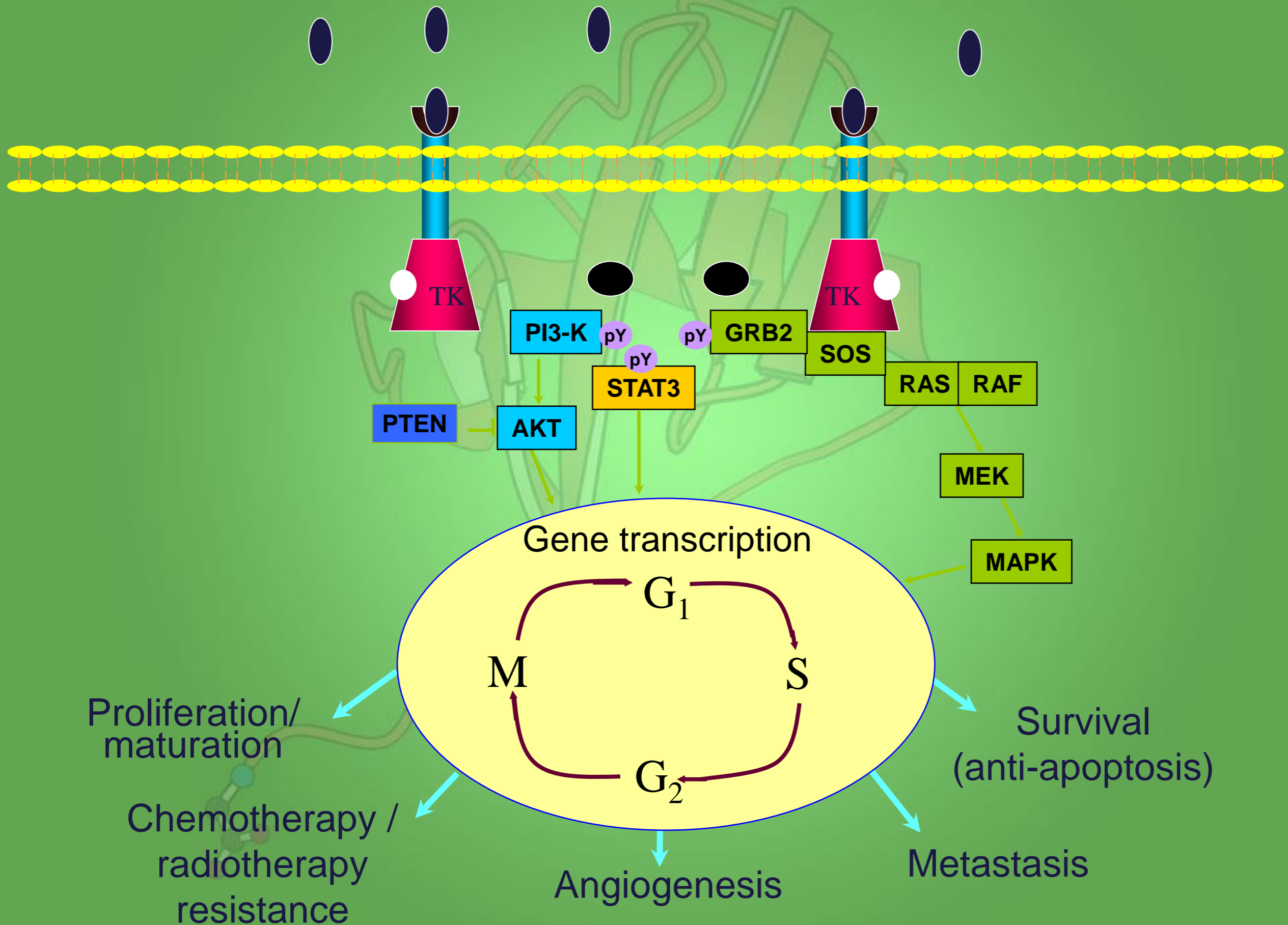
erbB3
HER3

erbB4
HER4

EGFR Function in Normal Cell



EGFR signal transduction in tumour cells



Strategies to inhibit EGFR signaling

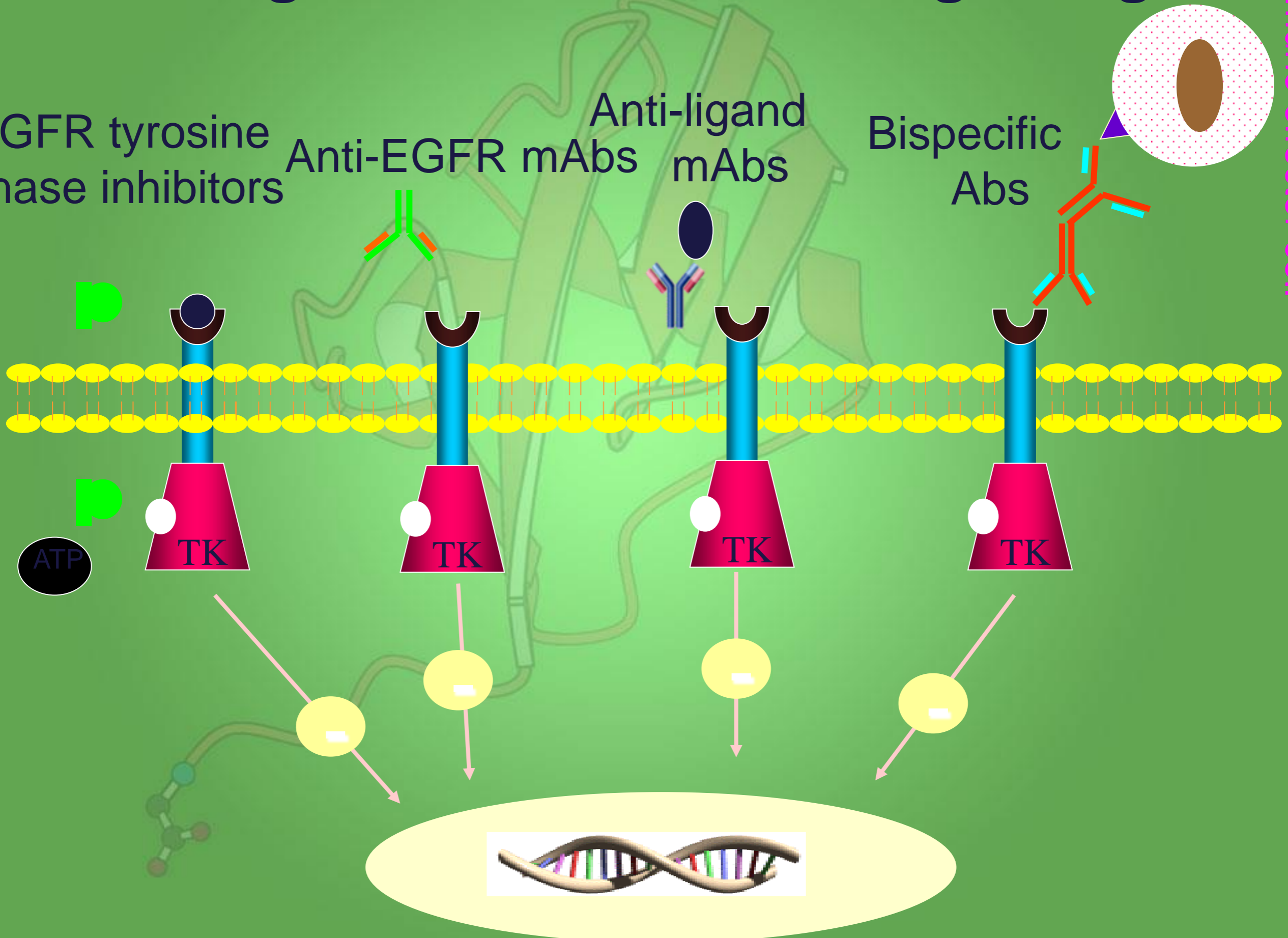
EGFR tyrosine kinase inhibitors

Anti-EGFR mAbs

Anti-ligand mAbs

Bispecific Abs

Immune effector cell



Transforming Growth Factor β (TGF β) Signals

- A large class of molecular signals involved in regulating development (bone growth, mesoderm formation, formation of cell-adhesion molecules and anti-proliferation effects).
- The activated TGF β receptor directly phosphorylates a transcription factor.

Human TGF β Signal Molecules

Three tissue-specific isoforms:

□ TGF β - 1

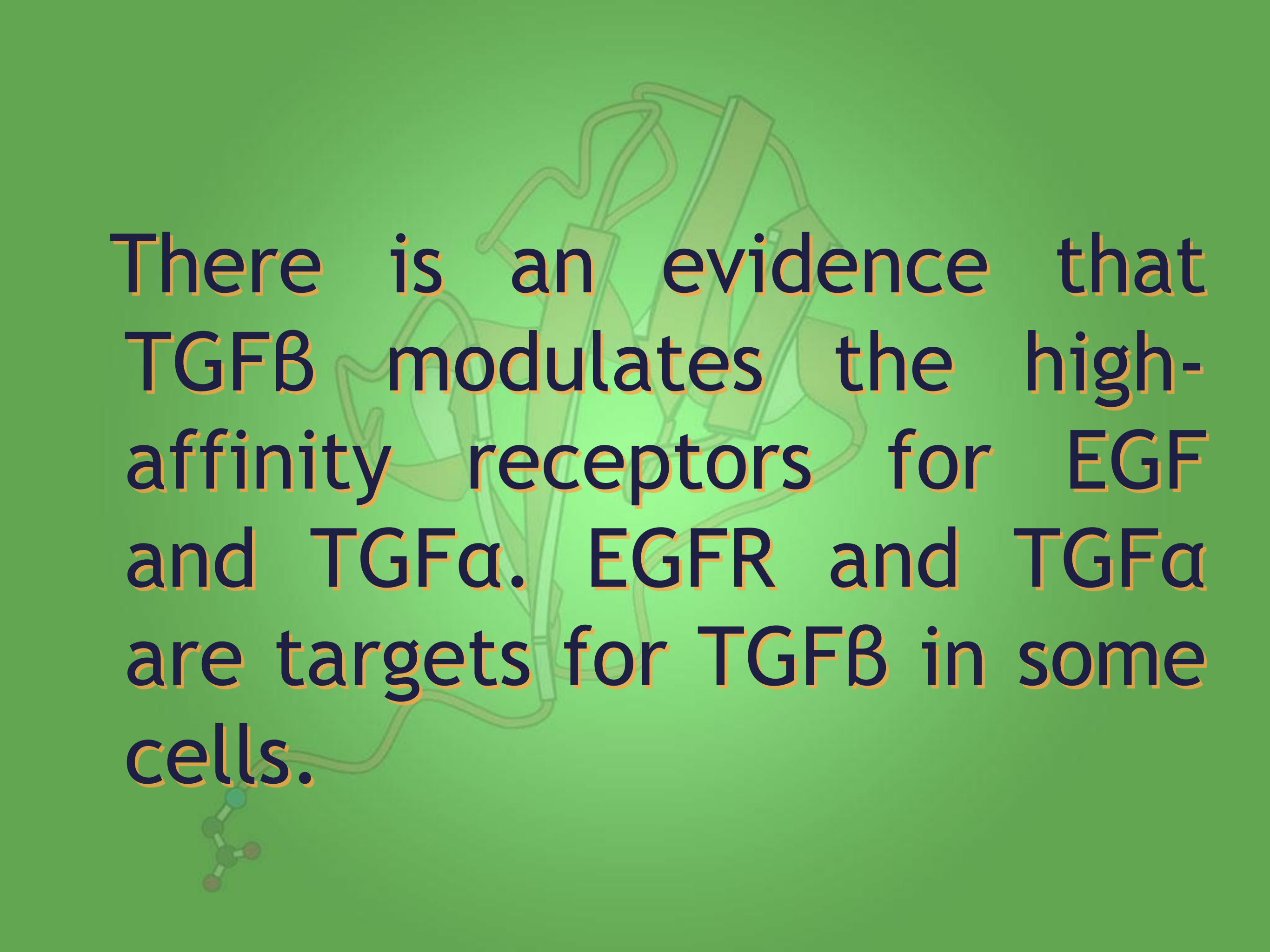
□ TGF β - 2

□ TGF β - 3

□ Dimeric homo- or hetero-
forms.



TGF β -1 is a multifunctional cytokine involved in the regulation of growth and differentiation of both normal and transformed cells. It has been reported that TGF β -1 mRNA and its protein were overexpressed in hepatocellular carcinoma tissues.

The background features a faint, light green illustration of a protein structure, likely a receptor, with various loops and helices. In the bottom left corner, there is a small, detailed molecular model showing a chain of atoms connected by bonds, with different colors representing different elements (e.g., carbon in grey, oxygen in red, nitrogen in blue).

There is an evidence that TGF β modulates the high-affinity receptors for EGF and TGF α . EGFR and TGF α are targets for TGF β in some cells.

Protein Tyrosine Kinases (TKs)

Receptor tyrosine kinases (RTK)

- **insulin receptor**
- **EGF receptor**
- **PDGF receptor**
- **TrkA**

Non-receptor tyrosine kinases (NRTK)

- **c-Src**
- **Janus kinases (Jak)**
- **Csk (C-terminal src kinase)**
- **Focal adhesion kinase (FAK)**

Subfamilies of Receptor Tyrosine Kinases

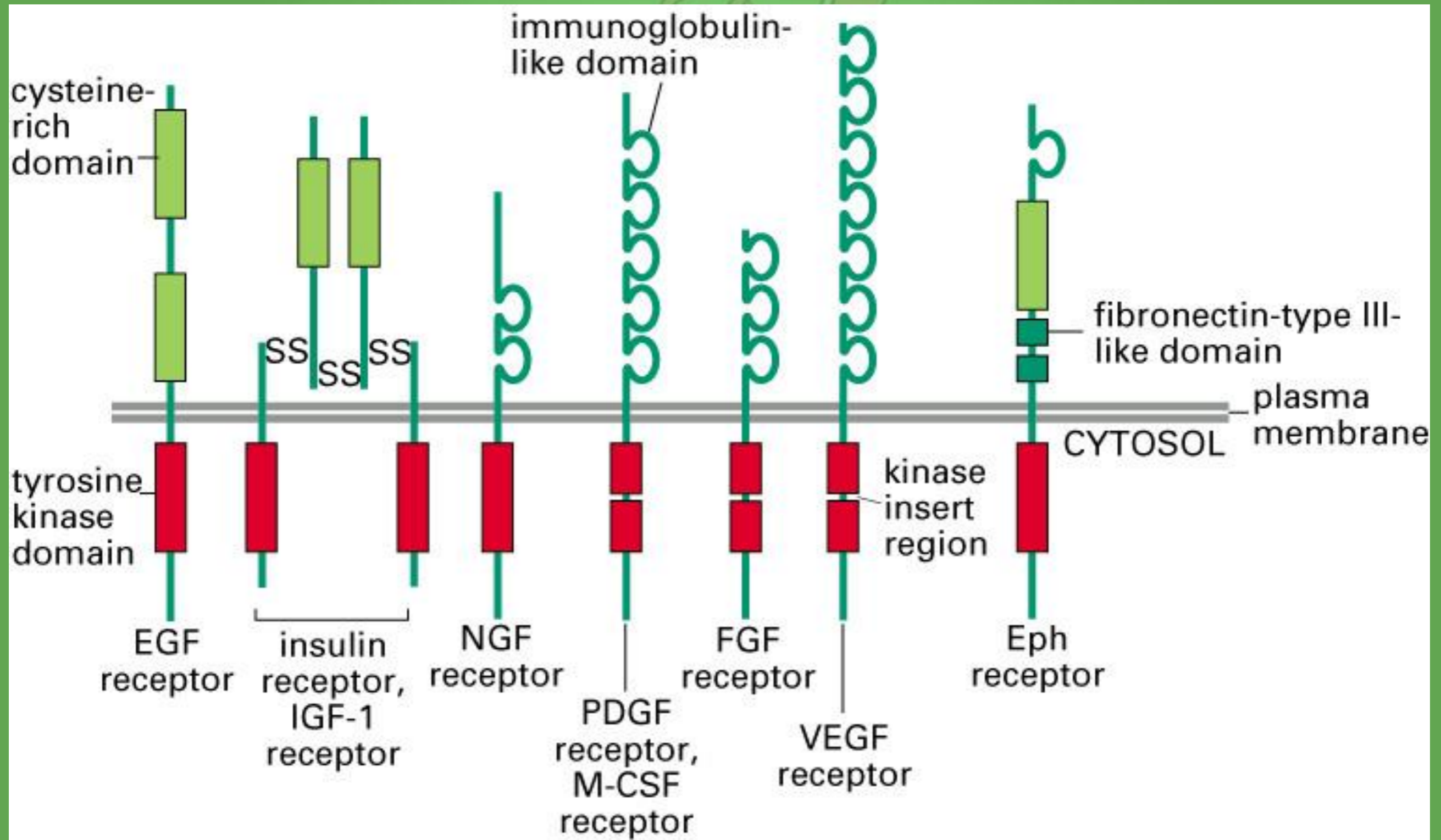


Figure 15-49. Molecular Biology of the Cell, 4th Edition.

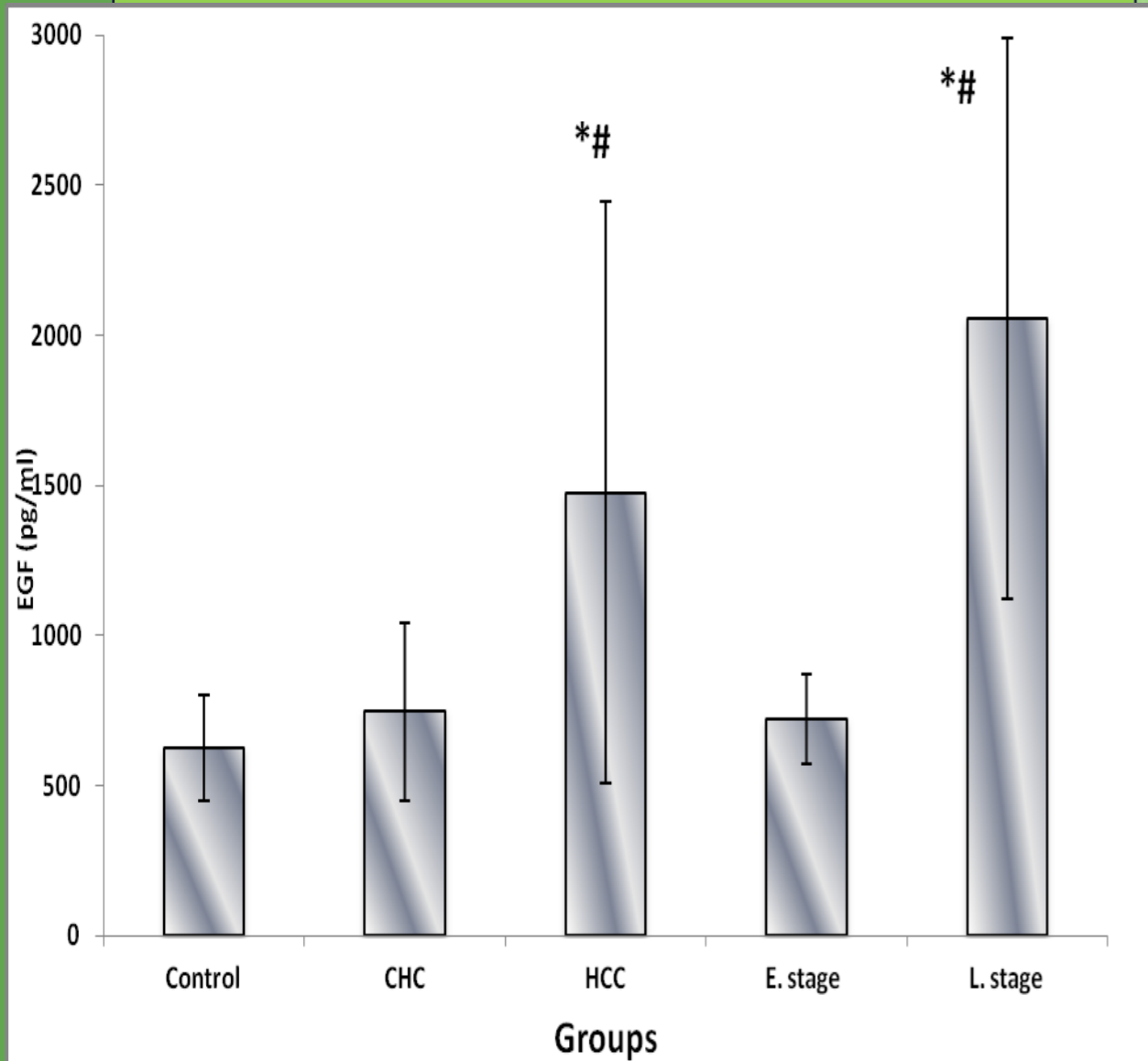
Evaluation of EGF, p-EGFR and TGF β -1

- Levels of EGF, p-EGFR and TGF β -1 in chronic hepatitis C (CHC) and hepatocellular carcinoma (HCC) patients in early and late stage of histopathological stages of HCC patients.
- EGF was determined by quantitative sandwich enzyme immunoassay technique. p-EGFR was determined by using PTK kit assay system (ELISA technique). TGF- β 1 was estimated using DRG TGF- β 1 ELISA technique.

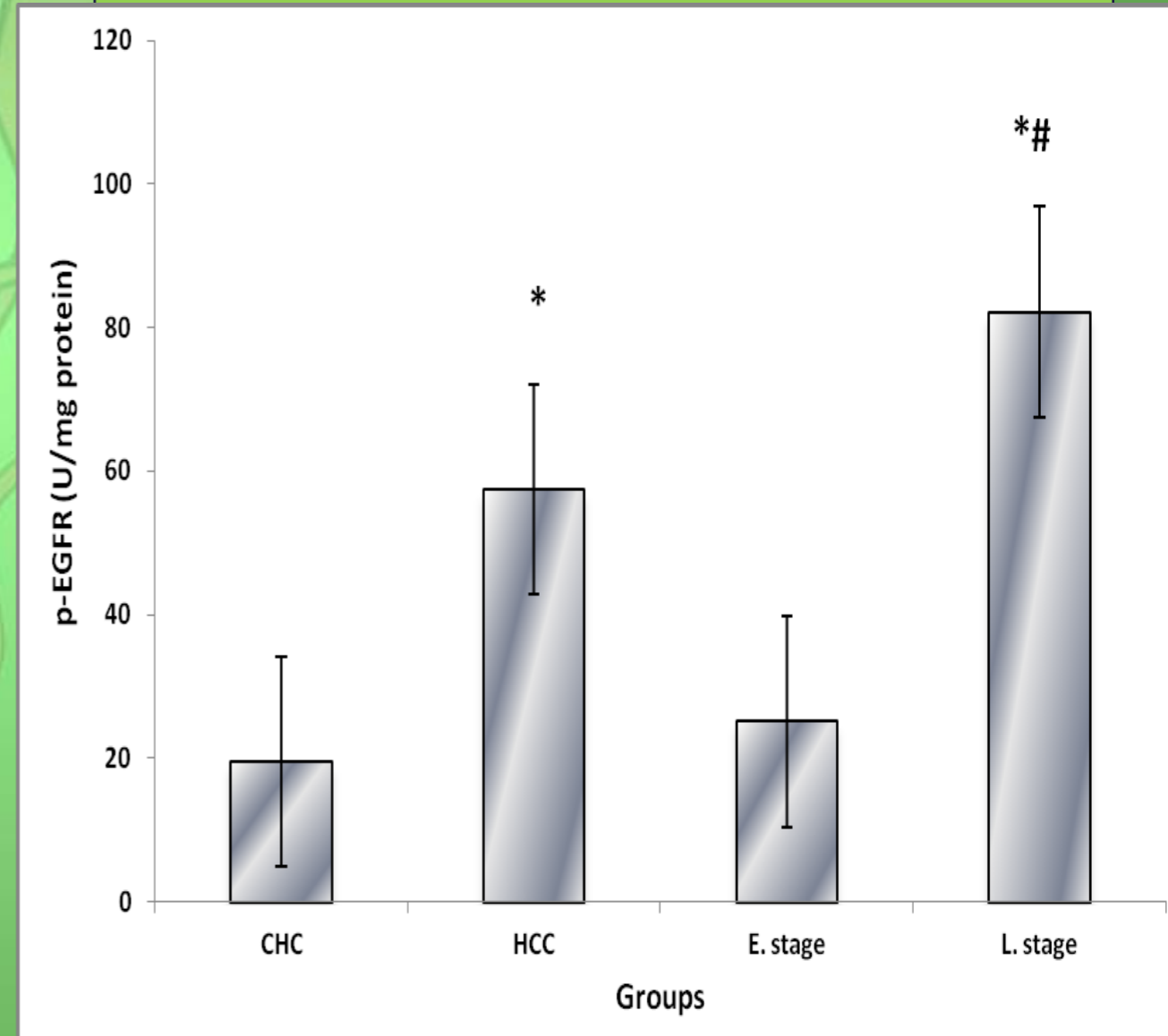
There are significant higher serum levels of EGF and TGF β -1 in patients with HCC compared to their level in patients with CHC infection and control subjects. The levels of p-EGFR in HCC and CHC patients show a highly significant difference between patients.

EGF and p-EGFR

EGF

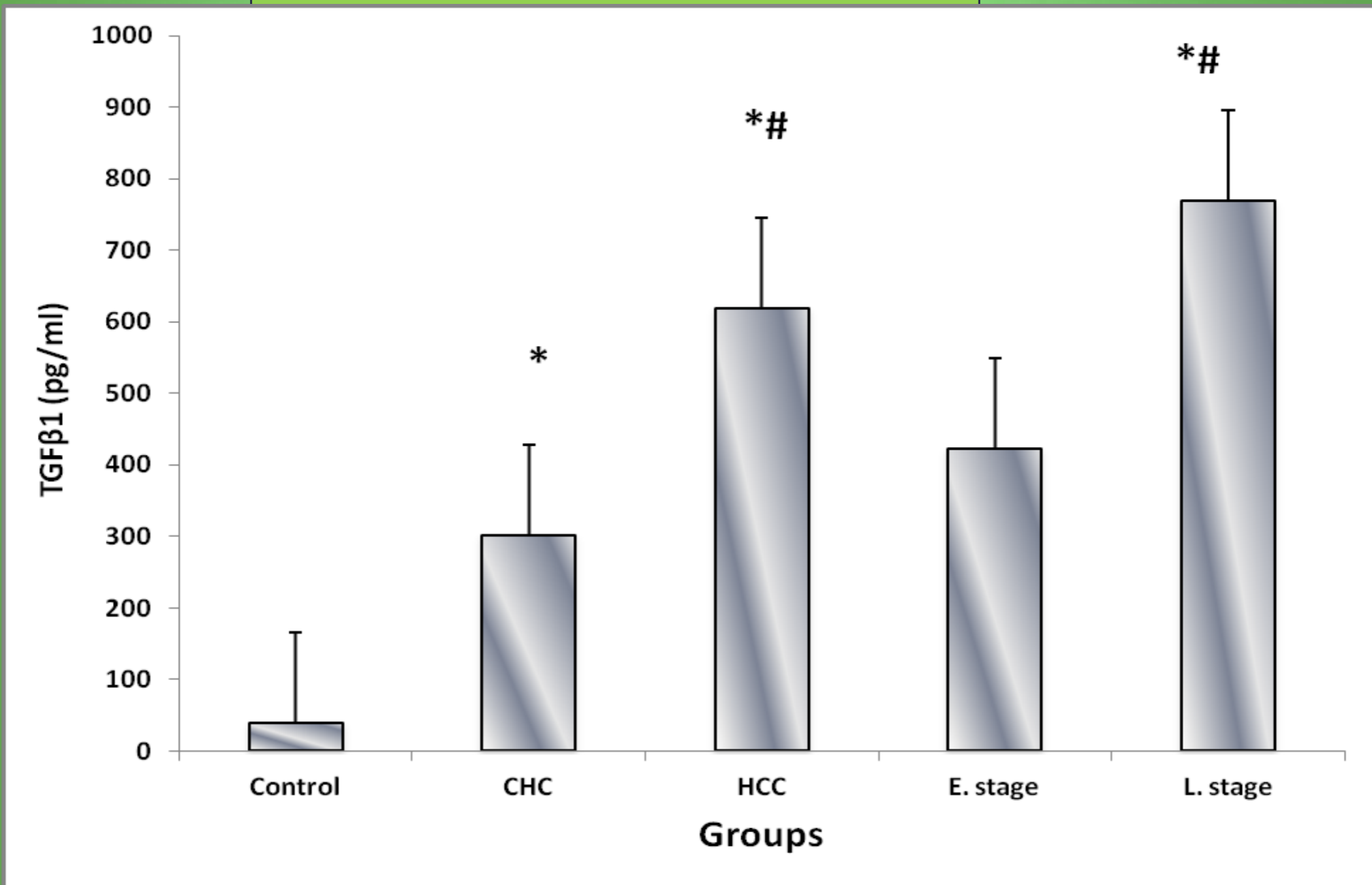


p-EGFR



Levels of TGFβ-1

TGFβ-1



Level of serum alfa-fetoprotein (AFP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and albumin of patients having HCC and CHC compared to control subjects.

Variable	Control (n = 20)	CHC (n = 20)	HCC (n = 30)
AFP (ng/ ml)	1.6 ± 0.26	23.5 ± 2.3*	445 ± 50.8*
ALB (g/dl)	4.6 ± 0.07	3.3 ± 0.06*	2.6 ± 0.05*
AST (U/L)	19.4 ± 0.4	76.4 ± 3.4*	58.5 ± 1.3*
ALT (U/L)	15.6 ± 0.59	62.2 ± 4.97*	38.1 ± 1.65*

Conclusion

EGF and its receptor phosphorylated form could be used as sensitive biomarkers for the diagnosis and prognosis of HCV-induced HCC. In conclusion, various growth factors are involved in different biological processes, some of which have a clinical importance in disease.

References

- Balbaa, M., Bassiouny, K. and El-Ashry, E. S. (2008). **Current Trends in Medicinal Chemistry**, 5: 33-44.
- Shehata, F., Abdel Monem, N., Sakr, M., Kasem, S. and Balbaa, M. (2013). **Medical Oncology**. DOI: 10.1007/s12032-013-0673-x.
- Balbaa, M. (2013). **Biochemistry & Physiology: Open Access**, 2: 4, <http://dx.doi.org/10.4172/2168-9652.1000e118>.



THANK YOU

Let us meet again..

We welcome you all to our future conferences of OMICS
International

4th Annual Conference on European Pharma
Congress

June 18-20, 2016, Berlin, Germany.

<http://europe.pharmaceuticalconferences.com/>