

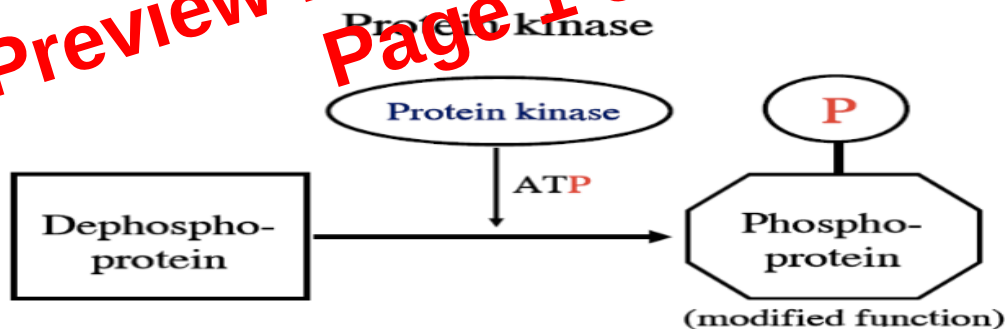
RECEPTOR TYROSINE KINASES: THERAPEUTIC TARGETS FOR CANCER

Introduction to RTKs:

1. **Cut. Burn. Poison.** – these are the conventional treatments for cancer today.
2. Cut – surgical removal of the cancer cells.
3. Burn – radiotherapy to remove the disease parts.
4. Poison – chemotherapy (medication).
5. However, these are not effective for all types of cancer and also have some harmful side effects.
6. Mapping of the human genome helped in the understanding and use of drugs that are more specific to the patient (**personalised medicine**) and to the type of cancer (i.e. use of **antibodies**).

Role in Carcinogenesis:

1. Cancer is a disease of **uncontrolled cellular proliferation**.
2. Normal cells receive growth factor signalling, which signals to the cell to begin proliferation, and additional signalling to **stop** proliferation. This limits the number of cells produced – the proliferative pool.
3. Cancer cells on the other hand, have an **excess of 'go' signals** due to the presence of oncogenes that either overexpress or activate the growth factor and receptors.
4. Additionally, these cells can also lose their 'stop' signals, i.e. loss of tumour suppressor genes, thus leading to the formation of malignant cells.
5. Growth factor signalling controls cellular processes:
 - Enzymatic activity modulates the function of different cellular genes, which are involved in different cancer.



6. **Protein phosphorylation/dephosphorylation** is the major mechanism of signal transduction within cells.
7. This is a post-translational modification – addition/removal of a phosphate group on serine, threonine and/or tyrosine residues.
8. There are also **non-receptor tyrosine kinases**, such as the ABL family, which plays a critical role in cancers (see later).