

# Cancer Essays

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# Outline

General 1B  
Essay Tips



Using the  
hallmarks as a  
framework



An example  
essay plan



Some bonus  
stuff for essays

# Some essay tips

- Practicing Essay Plans
  - 10 min per essay plan – trains speed
- Diagrams!
  - Aim for 4 diagrams per essay – saves you time writing out a long explanation sometimes
  - Inventive diagrams (that you have come up with yourself) will get you bonus marks
- Experimental Evidence
  - Lent – Defence against Pathogens lecture
- Catchy openers and closers
  - Quotes, broad themes, the sky is the limit!
  - Evolution is a good one generally
- Recycling 1A knowledge!
  - E.g. 1A apoptosis and cell cycle helps with cancer
- Bringing in information from other 1B subjects
  - Learning TCR signaling helps with both BOD and MODA/Pharm

# The hallmarks

- **Self sufficiency in growth signals**
- **Resistance to anti growth signals**
- Unlimited replicative potential
- **Evasion of apoptosis**
- Angiogenesis
- Metastasis
- **Genetic Instability**
- Altered Metabolism
- Tumour Promoting Inflammation
- **Evasion of the Immune System**

# Self Sufficiency in Growth Signals + Resistance to Apoptosis

- 2-fold logic to gaining self-sufficiency
- Good opportunity for a diagram! (spoiler alert for the next slide)
- Players I like to discuss
  - **Ras**
    - good link to why cetixumab doesn't always work
    - G12C Ras direct inhibitors -> pros and cons
  - **B-Raf** - nice link to vemurafenib and KIAA1549 tandem duplication
  - **Akt** – link to apoptosis
- **Bad** – pro-apoptotic BH3 only family member, inhibited by Akt phosphorylation
- Logic of resistance to apoptosis?

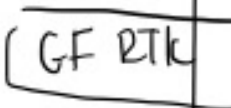
dabrafenib, trametinib



Plasma membrane

cetuximab

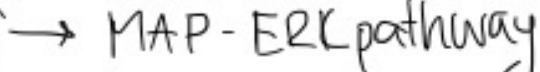
Growth factor (GF)



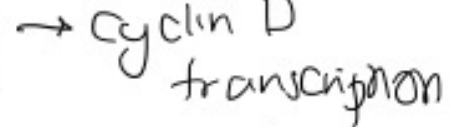
Ras



B-Raf



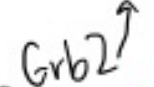
MAP-ERK pathway



cyclin D transcription



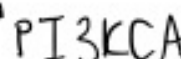
Sos1



Grb2

kinase inhibition

erlotinib  
gefitinib



PI3KCA

PIP<sub>2</sub>



PIP<sub>3</sub>



Akt

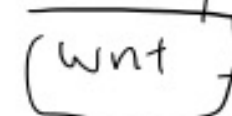
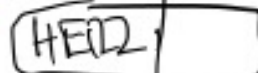


Bad

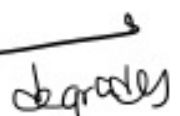


PTEN

trastuzumab



APC

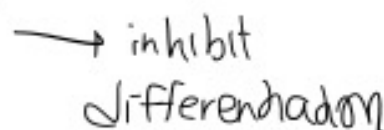


degrades

B-catenin



Tcf4



inhibit differentiation

cell cycle activation



# Resistance to Anti-Growth Signals

- **P53** is a nice tie in from resistance to apoptosis
- Get a nice big diagram in your head for p53 actions
- Dominant negative effect v two hit hypothesis
- **CDKN2A** – an evolutionarily strange gene
- **TGF-B** signalling is also useful to mention if you have time

# Evolutionary Links

- Reduced antigrowth and apoptotic signaling – increased proliferation and fraction of allele pool occupied -> p53
- Self sufficiency in growth signals and resistance to antigrowth signals – time for a metaphor!



# Metastasis

- Survival in a new environment - bottleneck
- Weiss retransplantation experiment
- **E-cadherin** -> link to antigrowth signals as well

# Genetic Instability

- Mutations beget mutations
- Lottery tickets
- Acquisition of more and more mutations, contributing to the other hallmarks
- Can discuss **BRCA2**, **Olaparib**, and emergence of PARP inhibitor resistance

# Evasion of the Immune System

- Immunotherapy – e.g. checkpoint inhibitors (good opportunity for a diagram!)
- Priming vs Activation Steps
- A panacea?

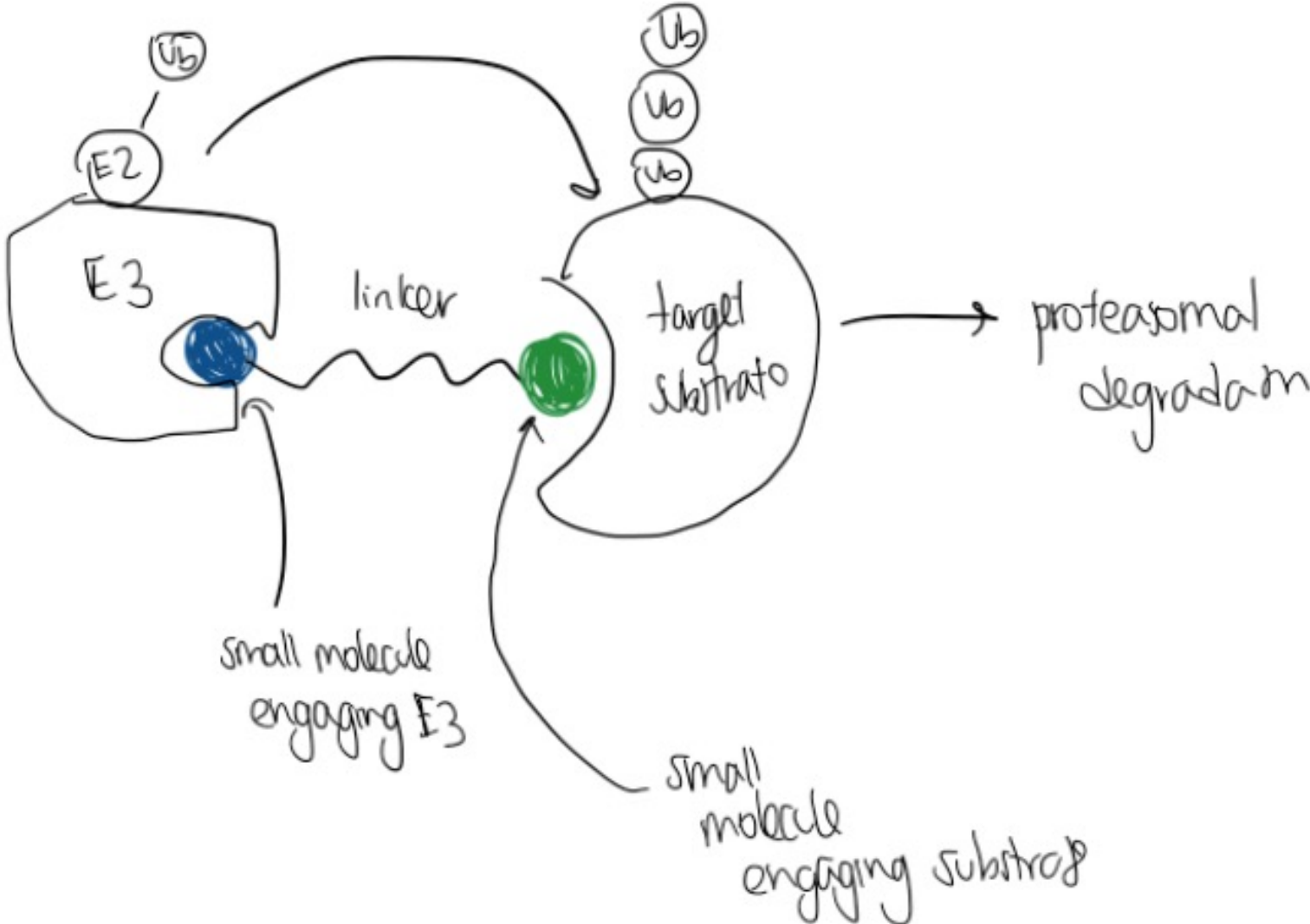
# Some things to keep thinking about

- How can exploit the hallmarks for therapeutic modulation
- E.g. oncolytic viruses for resistance to anti-growth signals, checkpoint blockade for evasion of the immune system, EGFR inhibitors for self-sufficiency in growth signals
- Links to evolution – how is this helping the tumour evolve?

Some extra stuff from  
Part II Pharmacology



# PROTACs



# Antibody Drug Conjugates (ADCs)

- 2 components
- An antibody which allows targeting of the ADC to specific targets
- A drug which specifically acts on target cells





# Example Essay Plan – Discuss how cancer develops as a result of dysregulated cellular signaling

- Intro – explain why dysregulated cell signaling helps cancer cells
- Growth Signals (self-sufficiency)
- Resistance to Apoptosis
- Anti-Growth
- Genetic Instability (as a driver)
- Conclusion – sometimes nice to end with which aspects you think are most important
- Remember – keep linking concepts to clinical utility, evolution etc

Thank you for your time!