Lecture 34 – Cell Cycle Control and Cancer Genetics

I. Cancers result from genetic alterations
   A. majority of cancers caused by somatic mutations
      1. spontaneous mutations
      2. environmental mutagens
         - UV light increases risk of skin cancer
         - cigarette smoke increases risk of respiratory tract cancer
   B. some predispositions to cancer are inherited
   C. definitions
      1. oncogene
      2. proto-oncogene
      3. viral or cellular oncogenes
      4. tumor suppressor

II. Hallmarks of cancer
   A. excessive cell proliferation
   B. metastasis
   C. an overview:

III. Cell cycle regulation
   A. Phases of the cell cycle
      1. G1 – Gap between end of mitosis and DNA synthesis
      2. S – DNA replication occurs
      3. G2 – gap between DNA synthesis and mitosis
      4. M – mitosis and cytokinesis
B. How to study cell cycle control:

C. Cyclin-dependent kinases ensure proper cell cycle timing
1. yeast mutants identified cell-division cycle (CDC) genes

D. regulation of cell cycle
1. several important points in cycle (2 shown)
   - regulated by activity of dimeric protein complex
   CDK = cyclin dependent kinase (kinases add phosphate to target proteins)
   cyclin = protein whose level changes through cell cycle

- why yeast?
  - similar cell-cycle control system as humans
  - reproduce rapidly
  - genes can be deleted, replaced or altered
  - can proliferate in haploid state
2. Cyclin/CDK regulate cell cycle transitions
   - cells use four classes of cyclin/CDK complexes

3. other proteins regulate CDK:cyclins, or are regulated by them

- how do checkpoints work?
  - consider DNA damage before S

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Rb = \text{retinoblastoma (a tumor suppressor)}
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E2F = \text{transcription factor}
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CDK = \text{cyclin dependent kinase}
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cyc = \text{cyclin}
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p53 = \text{tumor suppressor}
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p21 = \text{CDK inhibitor}
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IV. Apoptosis – programmed cell death
   A. excess cells produced during development destined to die
      - example: webbing between digits
   B. cells that may become cancerous also can be killed by apoptosis
      - better to lose a few cells than to develop cancer
      - intracellular proteases degrade proteins, kill cell
        - caspases
        - initial signal may be from outside cell or inside
   C. Two interconnected cell death pathways

V. Cancer
   A. Major human medical problem
   B. Cancers are descendants of one cell, accumulate mutations
   C. Cancer typically requires multiple mutations
      - best understood in colon cancer because intermediates isolated
   D. various types of cancer – promoting genetic alterations
      1. point mutations
      2. loss of domains
      3. gene fusions
      4. misexpression
5. extensive chromosome abnormalities common in cancers

E. Familial cancer syndromes
   1. some result from mutation in DNA repair genes

2. familial adenomatous polyposis coli (FAP)

3. Li-Fraumeni syndrome