Colorectal cancer (CRC) in humans and animals

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Background

- Third most common → 1 in 20 will develop
- Asymptomatic/non-specific
- Risk factors:
  - Endogenous (e.g. age, IBD)
  - Exogenous (e.g. obesity, diet)
- Screening

Hereditary CRC

- Hereditary nonpolyposis colon cancer (HPNCC)
  - Autosomal dominant
  - Defective DNA mismatch repair proteins (MLH1/MLH2) → polyps
  - 80% lifetime risk
  - Early age of onset
- Inheritance of two defective copies of base excision repair gene (MYH) → 100% lifetime risk of CRC
- Rare → will not discuss further
IBD-associated and Sporadic CRC

Sporadic CRC

Sporadic CRC
IBD-associated CRC

Chronic inflammation
- ROS generated by neutrophils and macrophages,
- ↑ cell turnover

Abnormal # of chromosomes

Pre-dysplastic changes
- ↓ antigen Sialosyl-Tn

K ras
- CRC
- Microsatellite instability

↑ tumor suppressor gene Rb
- Uncontrolled cell growth in presence of DNA damage

CRC in animals

- Domestic animals
  - Dogs/cats
    - Differences in metastasis
    - Companion animals
- Captive wildlife
  - cotton-top tamarin
  - Marmoset wasting syndrome
- Free-ranging wildlife
  - beluga whales in St. Lawrence Estuary (Quebec)
  - ↑ incidence of GI cancers
  - Cause unknown
    - Long lifespan
    - Exposure to contaminants
    - Inbred
Take-home Messages

- Either form of CRC involves step-wise progression from normal to cancerous
  - Due to increasing burden of mutations
- Many, many different combinations of mutations can result in CRC
  - Difficulty in identifying outcome
  - Difficulty in treatment
- Importance of screening

Questions?