Development and Characterization of Chordoma Xenografts

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Goals of the Project

• To create an animal model (xenograft) of chordoma
• To understand the molecular characteristics of the xenografts
Methods

• Tumor will be harvested from every patient with a chordoma undergoing surgery at Johns Hopkins
• Single cell suspensions will be made, and cells will be implanted in immune deficient mice within 1 hour of surgery
• Some mice will be injected with tumor cells into muscle, and some will have tumor cells implanted into bone
• Tumors that grow will be analyzed for
  – Chromosomal abnormalities
  – Gene expression profiles

First Xenograft

• Tumor obtained from 50 year old man with sacral chordoma
• NOD/SCID/IL-2Rγnull mice injected within an hour
• Mice injected in the perisacral region
Tumor is Serially Transplantable

- First tumors arose after 8 weeks
- Subsequent tumors more aggressive – appear after 3-4 weeks
- No evidence of metastasis in any mice
- 10 generations so far

Tumor Histology is Unusual

Typical Chordoma

Xenograft
Tumor Expresses T Brachyury RNA

- T Brachyury is considered to be a specific marker of chordoma
- We were unable to demonstrate T brachyury protein is present in the xenograft
- Using a sensitive technique (PCR), we could show T brachyury RNA is present

The Tumor is of Human Origin

- Genomic DNA binds to human Single Nucleotide Polymorphism arrays
Gene Expression Profiling

• Long list of genes with very high expression levels
  – Tumor antigens (GAGE 2, 4, 5, 6, 7, 7B, 8)
  – Other tumor-related genes (SSX1, SSX3, HOXB9, CXCL5)
  – VEGFC, NRAS, CDKN3

Progress

• So far 6 tumors have been harvested under this protocol
• Only 1 tumor has created a xenograft
• We anticipate harvesting another 6 tumors
• Of the first 6, none were implanted in bone, so hopefully this change will increase the chances of creating more xenografts