

# Development and Characterization of Chordoma Xenografts

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## Goals of the Project

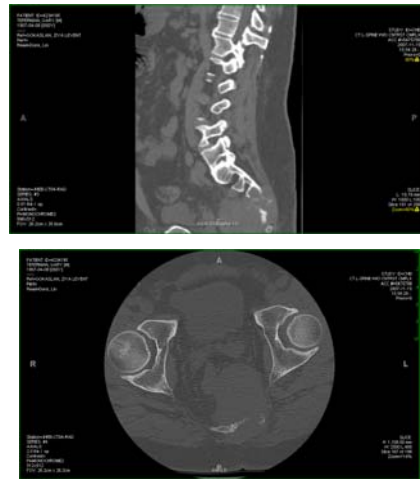
- To create an animal model (xenograft) of chordoma
- To understand the molecular characteristics of the xenografts

## 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

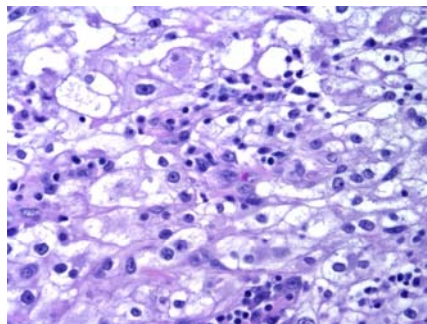
- Tumor obtained from 50 year old man with sacral chordoma
- NOD/SCID/IL-2R $\gamma$ <sup>null</sup> mice injected within an hour
- Mice injected in the perisacral region



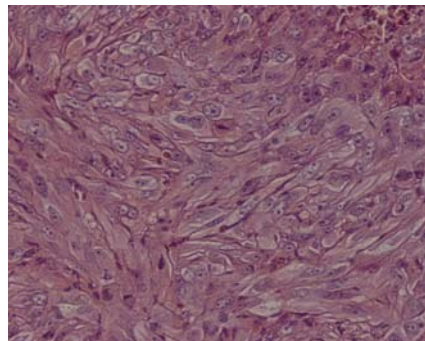
## Tumor is Serially Transplantable

- 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



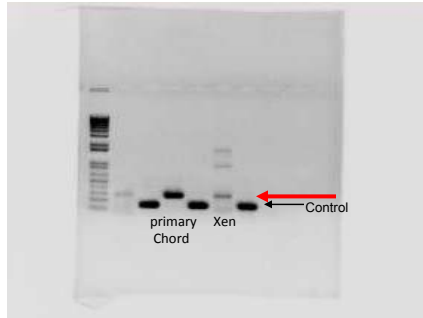
Typical Chordoma



Xenograft

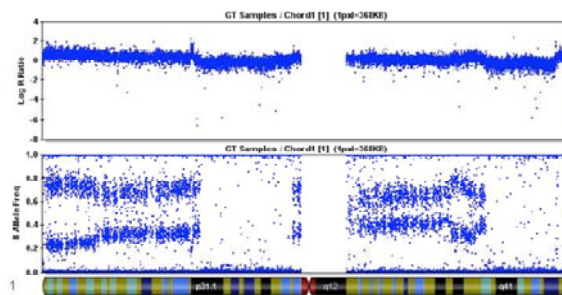
## Tumor Expresses T Brachyury RNA

- 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