Our mission is to rapidly develop effective treatments and ultimately a cure for chordoma.
A Revolution in Targeted Cancer Therapy

- “Cell Therapy Shows Promise for Acute Type of Leukemia” – New York Times, March 2013

- “New Lung Cancer Pill Highlights Improved Way of Treating Patients” – ABC News, August 2011

- “Drugs hailed as a 'major breakthrough' in treating deadly skin cancer” – Los Angeles Times, June 2011

- “FDA Approves Bayer Drug Stivarga for Rare Gastrointestinal Tumor” – Fox Business News, Feb 2013
How do we bring these advances to chordoma?
Goal line is demonstrated effectiveness in chordoma patients

“Humans are the best model of human disease”

But which treatments should be tested in chordoma patients?
Our strategy is to catalyze research at each step in the treatment development process, from start to finish, until a cure is found

1. Create the conditions needed for chordoma research to flourish – “enhanced serendipity”

2. Chart a path to new treatments - a “research roadmap” – and proactively marshal the resources, funding, and people needed to drive that research forward
Path towards a cure?
Needs of the research community?
Scientific Advisory Board

Neil Spector, MD
Director, Translational Research in Oncology, Duke Comprehensive Cancer Center

Michael Kelley, MD
Associate Professor, Internal Medicine, Duke University; Chief, Hematology/Oncology, Durham VA Medical Center

Paul Meltzer, MD, PhD
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Chief, Genetics Branch, National Cancer Institute, National Institutes of Health

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Associate Professor of Neurological Surgery, University of Virginia

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Fran Hornicek, MD, PhD
Associate Professor, Orthopaedic Surgery, Harvard Medical School; Chief, Orthopaedic Oncology Service at the Massachusetts General Hospital; Director, MGH Harris Center for Chordoma Care
Needs Identified

- **Models**
  - Cell lines
  - Xenografts
  - Transgenic models

- **Biospecimens**

- An understanding of the genetic variants and signaling pathways that drive chordoma

- **Testing of potential therapies in preclinical models**
  - Empirical screening, starting with approved drugs
  - Hypothesis driven testing

- **Funding for investigator-initiated, hypothesis-driven research**
Research Roadmap

Resource Development

- Clinical Data
- Biospecimens
- Cell Lines
- Xenografts
- Transgenic Animals

Discovery

- Genetic Epidemiology
  Familial Chordoma Study
- Multidimensional Genomics
  Expression | Rearrangements
  DNA Sequence | miRNA
- Functional Proteomics
- High Throughput Screening
  Approved Drugs | Combinations
  Novel Compounds | RNAi

Target Identification

- Integrated Data Analysis

Translation

- Biomarker Discovery
- Investigate Relevant Genes and Pathways

- Assay Development
  Cell line Testing
  Animal Testing
  Clinical Trials

Improved Treatments and Ultimately a Cure
CF Research Initiatives
Cell Line Repository

- **Goal:** 10 validated chordoma cell lines available through a central repository

- **Status:**
  - 3 validated cell lines (U-CH1, U-CH2, MUG-Chor1) available through CF, distributed by Kelley Lab
  - Distributed to **50+ labs**
  - Additional cell lines in development

- **Next steps:**
  - Facilitate acquisition, validation, deposit of 7 new cell lines
  - Award 7 additional prizes
  - Genomic characterization of all cell lines
**PDX Model Repository**

- **Goal:** 5 patient derived chordoma patient derived xenograft (PDX) models available through a central repository

- **Status:**
  - 3 PDX models developed, several in development
  - Partnership with Jackson Laboratory PDX repository

- **Next Steps:**
  - Complete acquisition and award prizes for 3 existing PDX models, and new models as they become available
  - Genomic characterization of all PDX models
Model Prizes

- **Prize purse:** $10,000 prize for each new cell line or PDX model
  - $15,000 if split between 2 collaborating labs

- **Requirements:**
  - Meet validation criteria
  - Deposit in public repository
Collects tumor tissue and data from hospitals across the US and makes it available to qualified researchers around the world.
Biobank

- **Goal:** high quality tissue samples from >200 patients available through a central repository, available to the entire research community

- **Status:**
  - IRB-approved protocol to collect tissue, blood, and clinical data
  - Centralized repository established at the Ohio State University
  - Partner sites: **UCSF, UNC, BNI, and UPMC**
  - 373 samples from **53 patients**

- **Next steps**
  - Initiated new hospital partner sites
  - Recruit additional chordoma patients
  - Begin accepting applications for biospecimens in Q4 2013
Donating Tissue for Research

- Tumor tissue is critical for research needed to develop new treatments

- The Chordoma Foundation Biobank enables chordoma patients who have surgery anywhere in the US to support research by donating their tissue
  - Coordinates with hospitals to obtain tissue from upcoming surgery
  - Retrieves tissue that might be saved from past surgery

- Confidential, free, IRB approved, won’t interfere with medical care

- www.chordoma.org/biobank

biobank@chordoma.org
877-230-0164
Biobank Donors

- Donor referrals
- CF consented donors
- Donors with collected tissue

Graph showing data for different months from 1 to 12, with categories for donor referrals, CF consented donors, and donors with collected tissue.
Chordoma Genome Project

• Using the most advanced technologies to systematically reveal all of the genetic changes that drive chordoma and thereby identify new targets for treatment.
Approved Drug Repurposing

• Tested 2816 approved drugs in 2 chordoma cell lines
  • ~40 showed activity
• Combination screens among active compounds identified synergistic response for several compound classes.
• Currently testing top 10 drugs in 2 recently developed mouse models at Johns Hopkins University
Drug Screening Pipeline

Background

• Numerous ideas for additional drugs have been proposed

• Drug testing is much more efficient at scale
  • Models are dispersed, takes a long time to acquire and establish a model in a lab

• Reproducibility across multiple models is important to enable translation of results

Solution

• A centralized in-vitro and in-vivo screening pipeline to enable multiple agents to be tested against panels of PDX models
  • Enable investigators and companies to submit agents for screening, or to propose hypotheses to be tested
• Enable researchers to test hypotheses and begin new projects
• Apply new ideas and approaches
• Leverage additional funding sources (2/11 so far)
### Research Investment Plans

<table>
<thead>
<tr>
<th>Project</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Cell Line and Xenograft Repositories</td>
<td>$300,000</td>
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<tr>
<td>Biobank</td>
<td>$200,000</td>
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<tr>
<td>Drug Screening</td>
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<tr>
<td>Engineered Models</td>
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<td>Targeting Brachyury</td>
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<tr>
<td>Investigator Initiated Seed Grants (2 years)</td>
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<tr>
<td>Natural History Research</td>
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<tr>
<td>New Opportunities</td>
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</tbody>
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Immediate Research Needs

- **Models - $400K**
  - Finish developing repositories of cell lines and animal models, which are the critical building blocks of research needed to find new treatments

- **Drug Screening - $300K**
  - Expand ongoing drug screening to discover which drugs are most likely to be effective for chordoma patients and should be considered for clinical trials

- **Seed Grant - $300K**
  - Seize the momentum from the Fourth International Chordoma Research Workshop by funding researchers to pursue new ideas and begin new collaborations