BUILDING PARTNERSHIPS

TO FIND A CURE

Chordoma Foundation

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What is Chordoma?

CHORDOMA: ***A malignant bone tumor of the skull base and spine***

Facts:

- ***Affects people of all ages***
- ***Most frequent in skull base and sacrum/coccyx***
- ***300 patients per year in US (1 per million)***
- ***More frequent in men***
- ***Generally resistant to chemotherapy***
- ***Average survival is 7 years***

Mission and Principles

Our mission is to improve the lives of patients with chordoma by rapidly developing effective treatments, and ultimately a cure

- **Patients can't afford to wait for a cure; we will be proactive and outcome-driven**
- **We will lead a focused and strategic international research effort**
- **We will initiate, facilitate, and fund multidisciplinary, multi-institutional collaborative research projects**

Barriers to Research

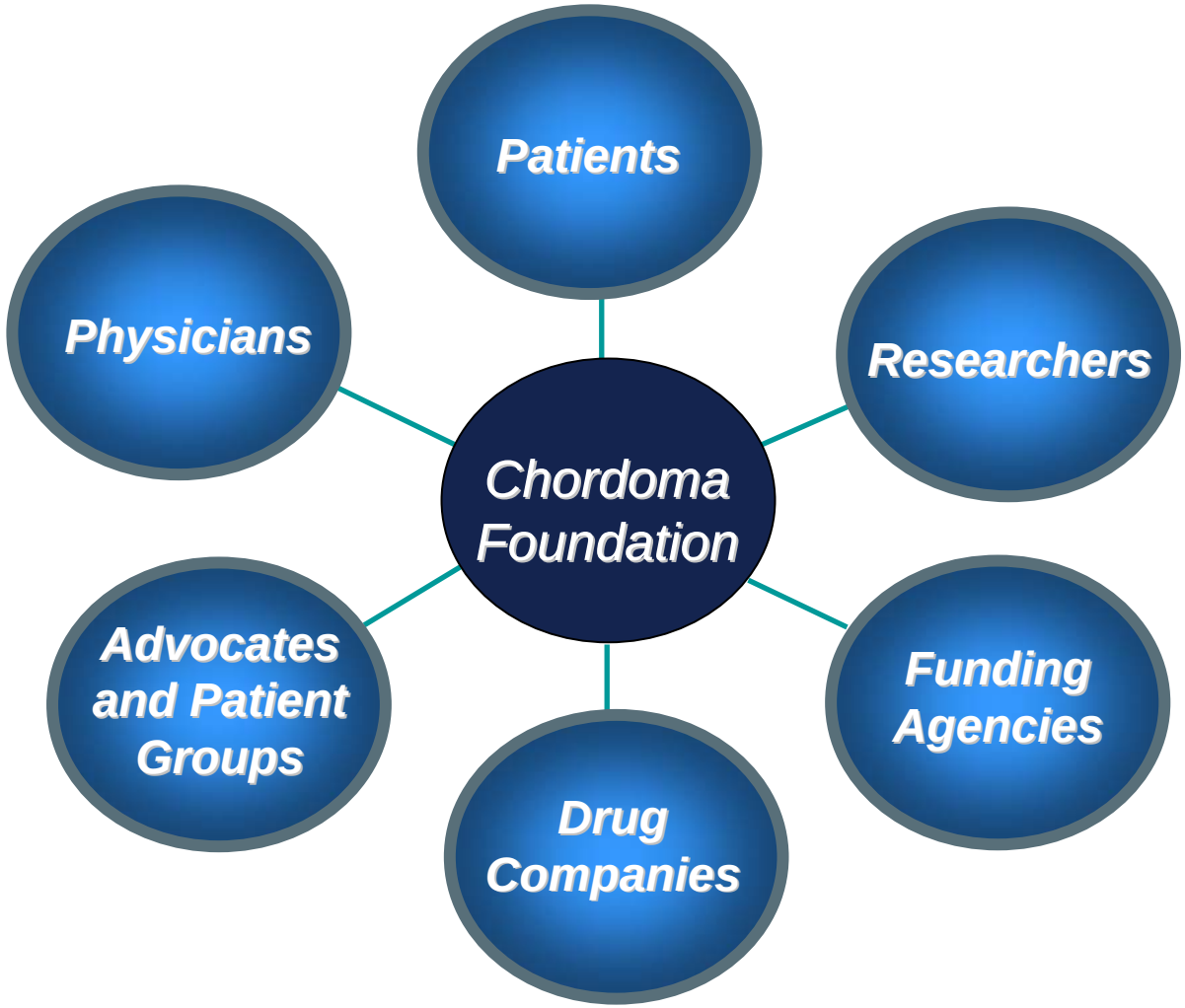
1. **Communication and Collaboration**
2. **Access to material and data**
3. **Funding**

Bridging all Stakeholders to Facilitate Research

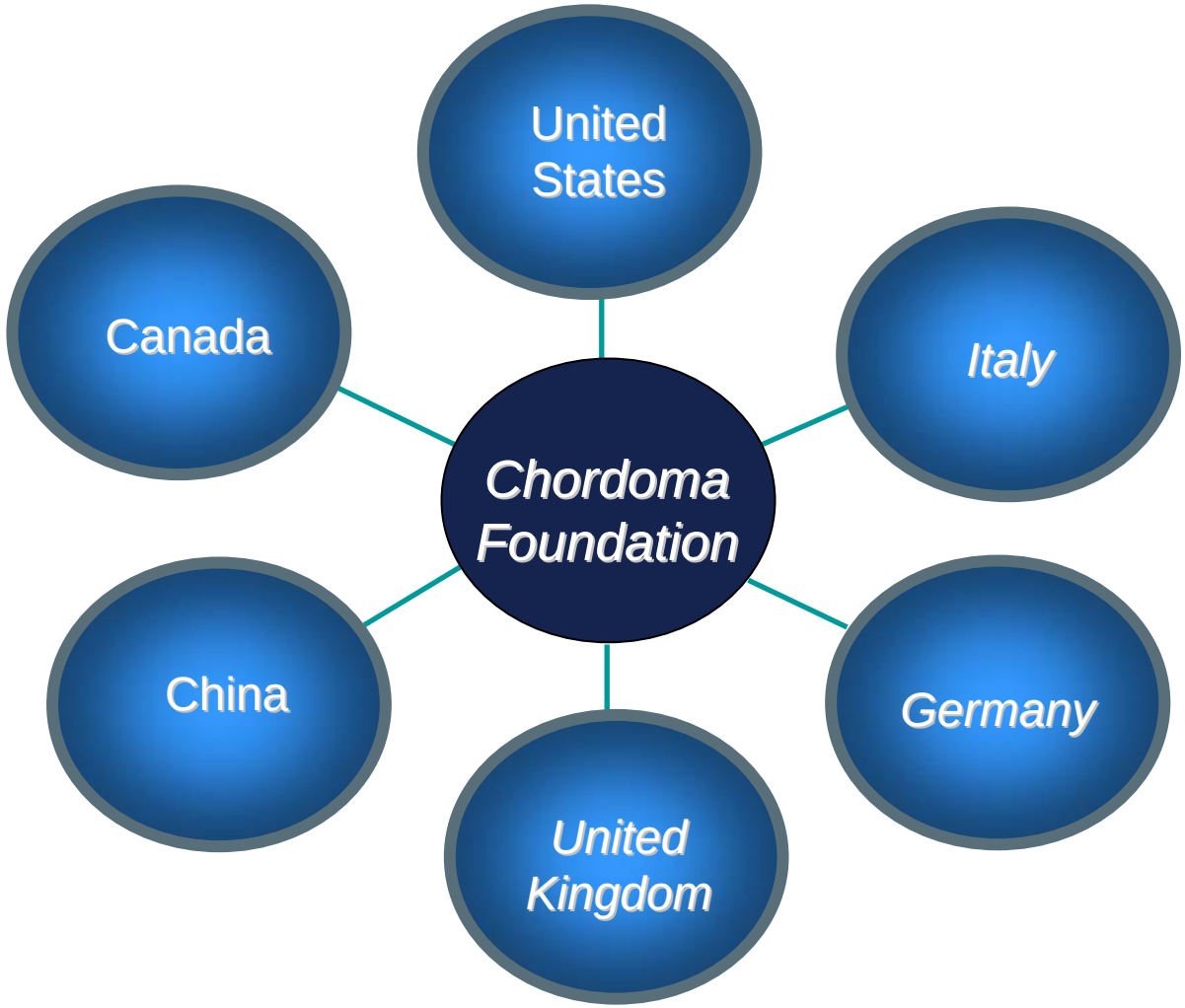
We coordinate collaborative projects between physicians and scientists to rapidly improve patient outcomes

The Chordoma Universe

Uniting Stakeholders



MULTI-NATIONAL



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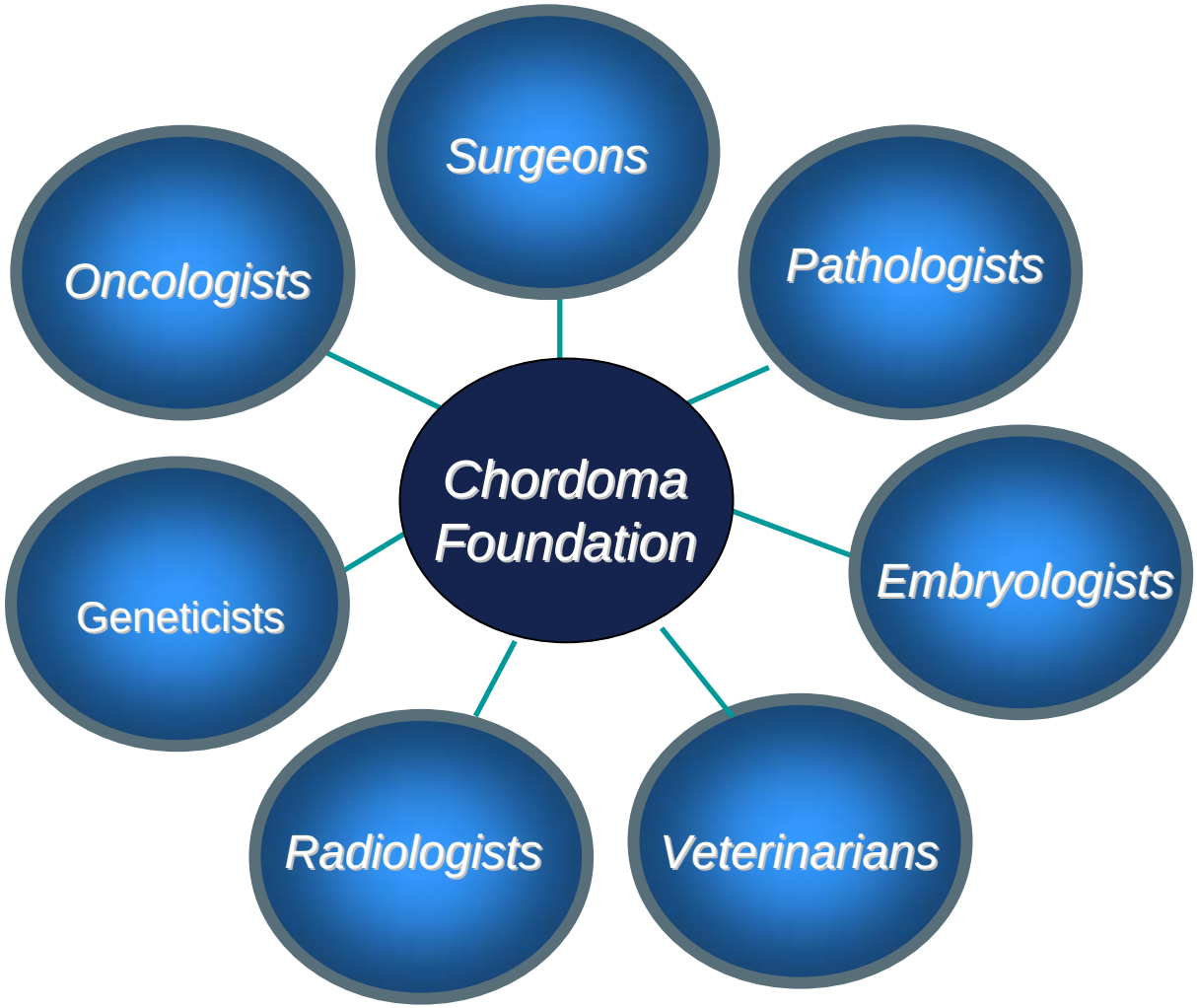
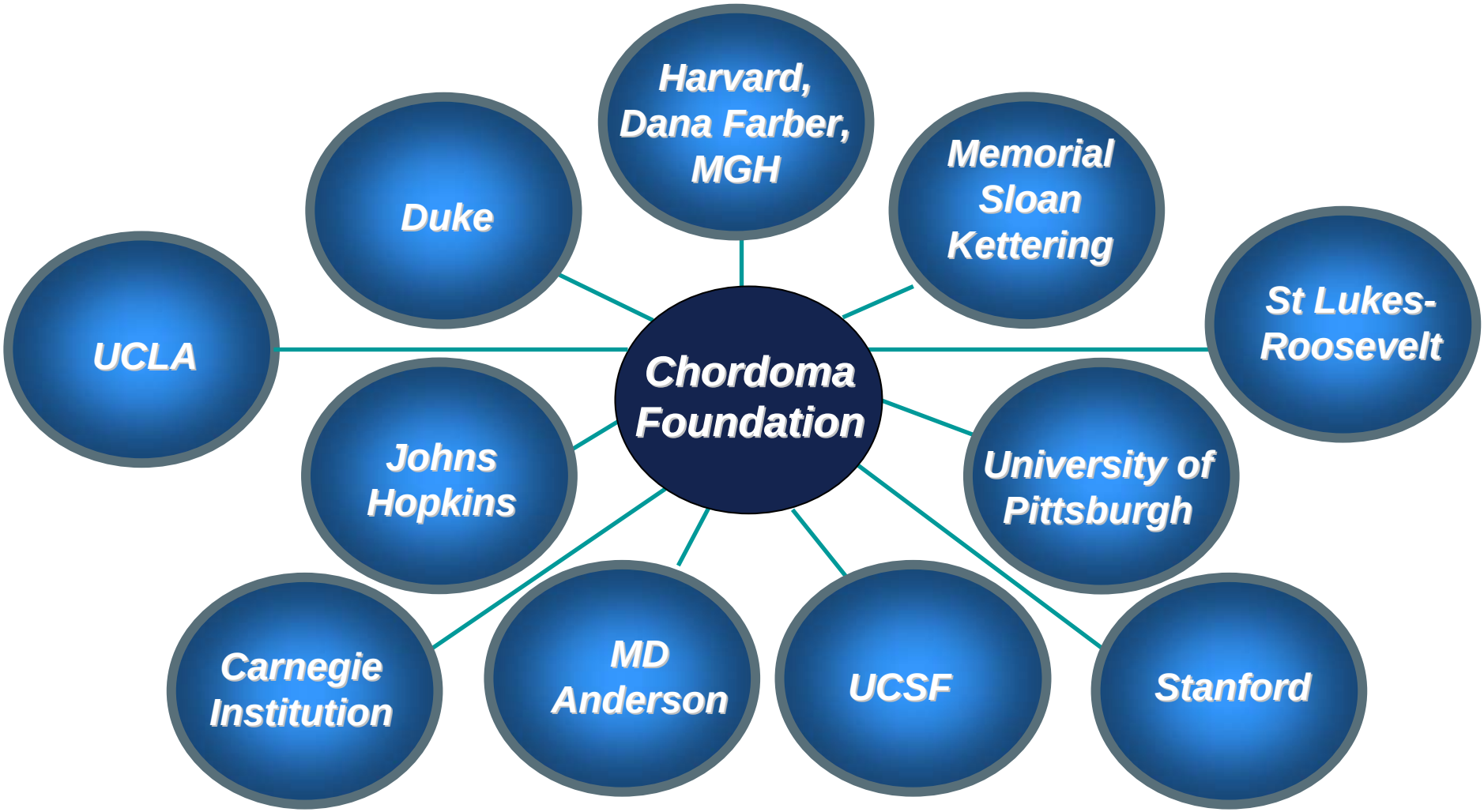
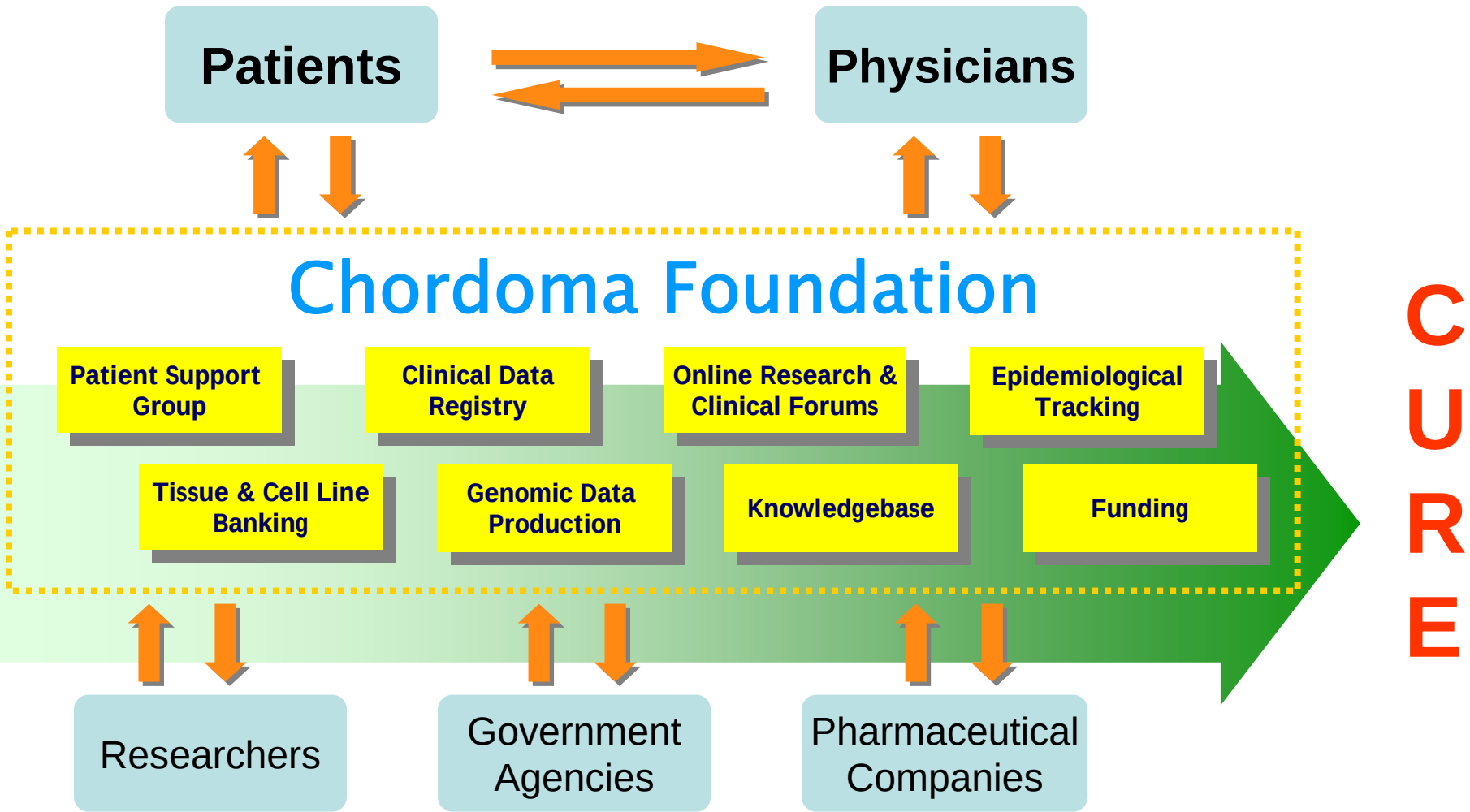


MULTI-INSTITUTIONAL



Catalyzing Translational Research



Services of the Foundation

For Researchers

- Opportunities for networking & collaborations
- Access to Biospecimens and Clinical Data
- Research Tools & Genomic Data
- Online Research Forum
- Curated Online Knowledgebase
- Patient Recruitment
- Funding and Grant Assistance

For Clinicians

- Educational resources & clinical care guidelines
- Opportunities for research collaborations & publications
- Secure Online Clinical Forum

For Patients

- Venue to directly support research
- Provide information, support, advice
- patient-based research and outcome tracking

Research Projects Underway

1) Gene expression analysis (Duke, MGH, MSKCC)
2) Genotyping and comparative genomic hybridization (NIH)
3) Examining the role of the TSC pathway in chordoma (Harvard)
4) In-vitro drug screening (NIH, Duke)
5) Using a melanoma antibody for therapy and targeted imaging (Memorial Sloan Kettering)
6) Exploring tractable signaling pathways (Duke)
   - HER family, wnt, hedgehog, PDGF, NFK-B, survivin
7) Exploring Ferret as an animal model
8) T-cell immune therapy (NIH)

Following Leads

In two cases of sacrococcygeal chordomas in individuals with TSC, we confirmed somatic inactivation of the corresponding wild-type allele by loss of heterozygosity analysis and immunohistochemistry. These data provide the first evidence of a pathogenic role by TSC genes in sacrococcygeal chordomas. – *Lee-Jones, et al., 2004*

Brachyury, a crucial regulator of notochordal development, is a novel biomarker for chordomas. – *Vujovic, et al., 2006*

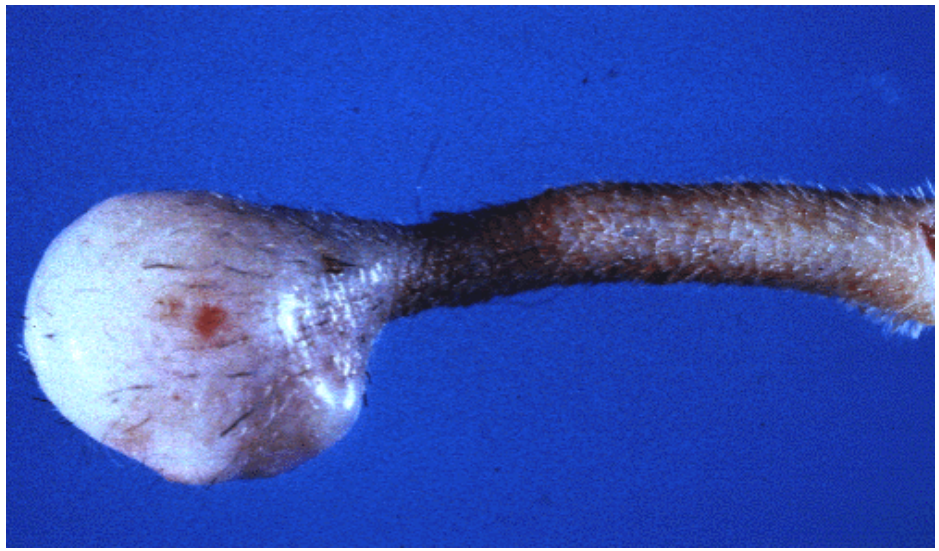
Taken together, the features of chordoma in ferrets outlined in this paper suggest that the ferret would be a good animal model for chordoma in human beings, particularly the chondroid variant. – *Dunn, et al., 1991*

Most chordomas had strong expression of both the hepatocyte growth factor/scatter factor receptor and EGFR. Inhibitors to EGFR are already in clinical use for other solid tissue tumors and represent a potentially viable experimental treatment option for refractory chordoma. Further studies are required to investigate these findings. – *Weinberger, et al., 2005*

What is Chordoma?

WILD ANIMAL MODEL:

chordomas occur in the tails of ferrets



First International Chordoma Research Workshop

Together we launched the first coordinated effort to cure chordoma

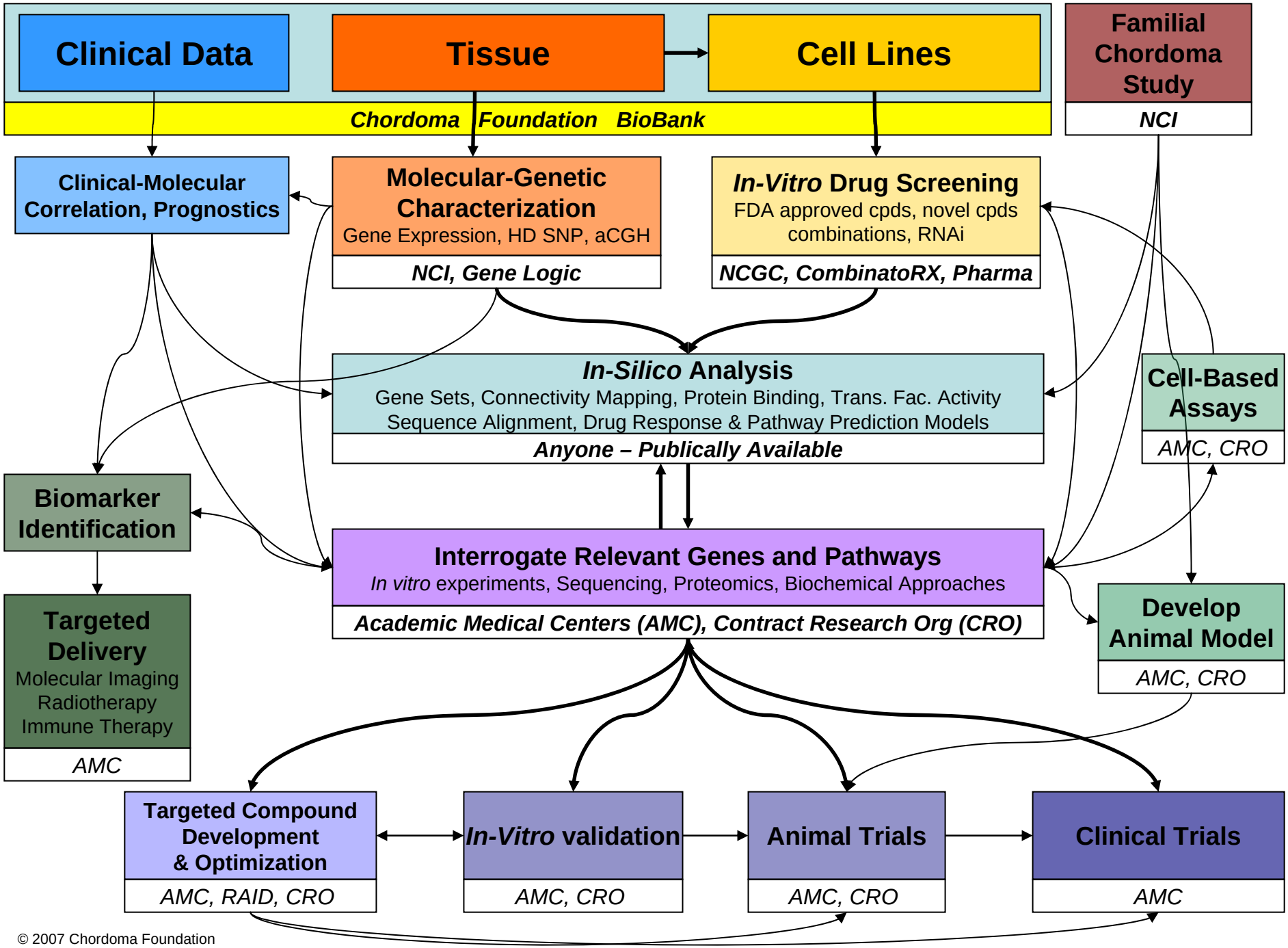
We invite you to join our team

Unanswered Questions

- What cells do chordomas arise from?
- Can methods of altering notochordal development be applied to chordomas?
- How are chordoma cells distinct from “normal” cells?
- What initiates tumorogenesis? What are the events that give rise to chordoma?
- Are there genes that increase susceptibility to chordoma?
- What drives their proliferation?
- What triggers metastasis? Why do some chordomas metastasize while others do not?
- What are the pathways (signaling network) regulating the growth and survival of chordoma, and are there tractable targets?
- Are chordomas in some patients permanently controlled with treatment?
- Why do these tumors require such high radiation doses for tumor control (i.e. would molecular profiling show upregulation of radiation repair genes?)
- Are there molecular or genetic factors that predict recurrence and/or metastasis?
- What will slow disease progression?
- Can a representative model system be developed to test the effectiveness of targeted therapies? Can we induce chordomas in animals?
- Does immunotherapy have any value in chordoma?
- Can we effectively deliver small molecules, antibodies, or imaging agents to chordoma?
- What is the most effective way to improve quality of life/outcomes of patients.

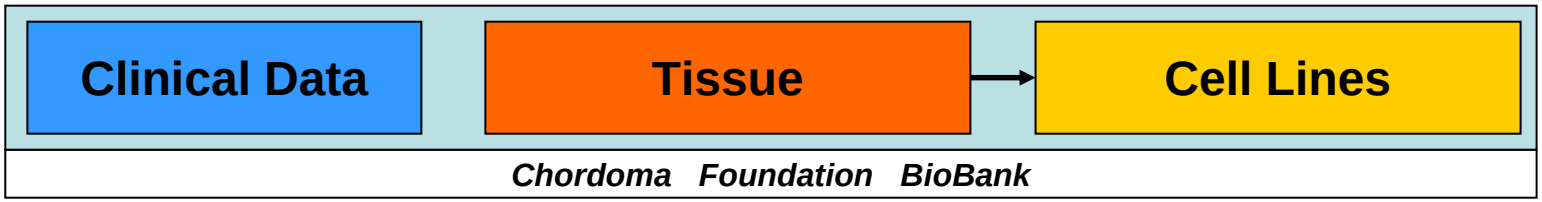
How to cure a disease?

- Traditional target identification and drug development takes >15 years
- Can short circuit this linear process by
  - Tracking off-label use
  - High throughput screening of FDA approved compounds
  - Identifying “already drugable” targets
  - Screen preclinical compounds for orphan indication
  - Piggyback clinical trials
- “*Multiple shots on goal*”



Immediate Research Priorities

- Create tissue procurement network
- Develop resources
  - Centralized biorepository (BioBank)
    - collect tissue, blood, urine and clinical data
  - Cell lines
  - Tissue microarrays
  - Xenographs
  - Animal model -- collect ferrets with spontaneous chordoma
- Recruit patients for Familial Chordoma Study
- Molecular-Genetic Tumor Characterization
  - Gene expression
  - High density SNP genotyping
- Empirical approach: screen cell lines against large compound libraries
- Interrogate known oncogene signaling pathways



- Dedicated internal Institutional Review Board
- HIPPA compliant consent forms, ability for re-consent
- Tissue Repository Information Management System (TRIMS)
  - Standardized nomenclature (SNOMED)
  - Suitable for FDA compliant clinical trials
- Secure online portal for collection of clinical data
  - Portable electronic health records
- Aliquoting and automated distribution
- Genomic services
  - DNA & RNA Extraction
  - Gene Expression
  - Genotyping (100K)

GENE LOGIC

Genetic Alliance BioBank

Phase I Fundraising Targets

Project	Fundraising Target
Host International Chordoma Research Workshops in 2008 and 2009	**$120,000**
Establish Chordoma Foundation BioBank (plus 2 years operation)	**$300,000**
Develop expert recommendations and treatment guidelines	**$50,000**
Provide seed grants to researchers	**$500,000**
Develop and validate standardized chordoma cell lines	**$100,000**
Develop chordoma animal model	**$300,000**
Create chordoma tumor microarray	**$80,000**
Genome-wide tumor profiling	**$250,000**
Targeted sequencing project	**$300,000**
High throughput drug screening	**$300,000**
Natural history and epidemiology study	**$100,000**
Research staff	**$200,000**
Total 2 year research budget:	**$2,600,000**
Management and administrative staff	**$300,000**
Operational, and fundraising costs	**$100,000**
Total 2 year operating budget	**$400,000**
2-Year Grand Total:	**$3,000,000**

HOW CAN WE HELP YOU?

NEXT ACTIONS?