Questions Posed by Participants

Mechanisms of Disease

1. What cell population do chordomas arise from?
2. What causes benign notochordal cell tumors (BNCT), and are these lesions proliferative?
3. What initiates tumorogenesis? Is there a consistent event that causes BNCT to transform into chordomas or are there multiple different events that can trigger malignant transformation?
4. Why do chordomas arise from within the bone and not the intervertebral disc? Is there some factor in the bone that causes notochordal cells to proliferate?
5. Are there one or multiple malignant cell types within a chordoma?
6. How do the malignant cells interact with cells in the microenvironment?
7. Why do chordomas characteristically form intralesional fibrous septae and lobules?
8. What explains the aggressive nature of chordoma despite slow growth?
9. What triggers metastasis? Why do some chordomas metastasize while others do not?
10. Are there molecular or genetic factors that predict recurrence and/or metastasis?
11. Why do these tumors require such high radiation doses for tumor control? Would molecular profiling show upregulation of radiation repair genes?
12. Can a representative model system be developed to test the effectiveness of targeted therapies? What model systems should we focus on?
13. What are the optimal growth conditions for chordoma cell lines?
14. What markers or criteria should be used to verify that a cell line comes from a chordoma?
15. What strategies could be used to induce chordomas in animals?
16. Why do ferrets have a higher incidence of chordomas? What is the value of ferret chordomas as a model for human chordomas?
17. Are there genes that increase susceptibility to chordoma?
18. What explains the co-occurrence of chordoma and Tuberous Sclerosis? Why have most cases of chordomas with TS been diagnosed in very young children? Are all or most pediatric chordomas a manifestation of TS?
19. Are pediatric chordomas biologically distinct from adult chordomas?

Questions Posed by Participants

20. What is the natural history of chordoma occurring in families with other cancers?

21. What explains the difference in survival based on gender? What explains the difference in anatomical distribution based on gender? Do sex hormones play a role in the initiation or progression of chordoma?

Therapeutic Development

22. What are the signaling pathways that regulate the growth and survival of chordoma?

23. Of the currently tractable drug targets, which play a role in chordoma?

24. What receptors are expressed and activated in chordoma?

25. Does immune therapy have any value in treating chordoma?

26. Can we effectively deliver small molecules, antibodies, or imaging agents to chordoma?

27. Why are chordomas resistant to cytotoxic chemotherapies?

28. Can radiation sensitizers be used to increase effectiveness of radiation?

Clinical Management

29. What is the optimal clinical management protocol for chordomas?

30. Does neoadjuvant radiation and/or chemotherapy improve clinical outcome?

31. Would adjuvant chemotherapy be beneficial even in cases of gross total resection?

32. What dose and form of radiation is optimal – protons, carbon ions, radiosurgery?

33. Are chordomas in some patients permanently controlled with surgery with or without radiation? What is the long term cure rate?

34. What are the most effective and quickest ways to improve outcomes and quality of life for chordoma patients?

35. Are there surgical approaches that minimize disability, while achieving the goal of complete resection?

36. What clinical trials are open to chordoma patients? Given the current understanding of the disease, what new trials are most rational?

37. How can early diagnosis be improved?

38. How can we facilitate early referral to specialists?