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## **Chondrosarcoma models : understanding chemoresistance mechanisms for use in targeted treatment**

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## Stellingen (Scientific Statements)

Behorend bij het proefschrift

*Chondrosarcoma Models: Understanding Chemoresistance Mechanisms for Use in Targeted Treatment*

1. Activity of anti-apoptotic Bcl-2 family members plays a role in the chemoresistance of chondrosarcoma. ***This thesis***
2. Heterogeneous tyrosine kinase signaling in chondrosarcoma poses a challenge for finding a uniform target and necessitates the development of personalized therapy. ***This thesis***
3. Combination strategies of conventional chemotherapy with new targeted therapeutics are key to overcoming chemoresistance in chondrosarcoma. ***This thesis***
4. Completion of the bench to bedside pipeline is a crucial step towards developing new treatment strategies for chondrosarcoma. ***This thesis***
5. From a clinical perspective, pretreatment with novel, potent Bcl-2 inhibitors, either alone or in combination with conventional chemotherapeutic agents, hold significant promise for providing beneficial clinical outcomes. ***Thomas, Expert Opin Ther Targets, 2013: 17(1):61-75***
6. Over the past 15 years, protein kinases have become the most important drug targets in the field of anti-tumor drugs. ***Cohen, ACS Chem Biol, 2013: 18(1):96-104***
7. Every step of the journey of a protein biomarker from the bench to the clinic needs to be meticulously planned and executed in order to succeed (***Pavlou, Clin Chem, 2013: 59(1):147-157***) and the development of new drugs relies heavily on animal studies to provide a framework for human clinical trials. ***Zhou, AAPS J, 2011: 13(1):111-20***
8. Phase I trials show well tolerability of dual inhibition using PI3K and MEK inhibitors which may be needed to treat cancers with driver mutations that cannot be directly targeted, such as mutational activation of RAS. ***Britten, Cancer Chemother Pharmacol 2013: 71:1359-1409***
9. There are things known and there are things unknown, and in between there are the doors of perception. ***Aldous Huxley***
10. You build on failure, you use it as a stepping stone. ***Johnny Cash***
11. An Fortschritt glauben heißt nicht glauben daß ein Fortschritt schon geschehen ist. (To believe in progress does not mean progress has been made) ***Kafka, Aphormismen II, 4***

Jolieke G van Oosterwijk

Leiden, 19 November 2013