



Universiteit
Leiden
The Netherlands

Exploiting vulnerabilities induced by recurrent mutations in chondrosarcoma and giant cell tumour of bone: therapeutic targeting of the altered epigenome and beyond

Venneker, S.

Citation

Venneker, S. (2023, January 10). *Exploiting vulnerabilities induced by recurrent mutations in chondrosarcoma and giant cell tumour of bone: therapeutic targeting of the altered epigenome and beyond*. Retrieved from <https://hdl.handle.net/1887/3505433>

Version: Publisher's Version

[Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3505433>

Note: To cite this publication please use the final published version (if applicable).

**Exploiting vulnerabilities induced by recurrent mutations
in chondrosarcoma and giant cell tumour of bone**

Therapeutic targeting of the altered epigenome and beyond

Sanne Venneker

Exploiting vulnerabilities induced by recurrent mutations in chondrosarcoma and giant cell tumour of bone: Therapeutic targeting of the altered epigenome and beyond
Thesis, University of Leiden, The Netherlands

ISBN: 978-94-6469-100-9

Cover Design: Iris Boelhouwer en Sanne Venneker

Layout and Printing: ProefschriftMaken | www.proefschriftmaken.nl

Printing of this thesis was financially supported by the Department of Pathology, Leiden University Medical Center.

Copyright © 2022, Sanne Venneker, The Netherlands

All rights reserved. No part of this thesis may be reproduced, stored, or transmitted without prior permission of the author.

**Exploiting vulnerabilities induced by recurrent mutations
in chondrosarcoma and giant cell tumour of bone**
Therapeutic targeting of the altered epigenome and beyond

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 10 januari 2023
klokke 13:45 uur

door

Sanne Venneker
geboren te Haarlem
in 1992

Promotores

Prof. dr. J.V.M.G. Bovée

Prof. dr. E.H.J. Danen

Co-promotor

Dr. K. Szuhai

Leden promotiecommissie

Prof. dr. M.J. Jager

Prof. dr. G. Sys (Universitair Ziekenhuis Gent)

Dr. I.M.E. Desar (Radboud Universitair Medisch Centrum)

Dr. J.J.L. Jacobs (Nederlands Kanker Instituut)

“Done is better than perfect.”

Sheryl Sandberg, Lean In: Women, Work, and the Will to Lead, 2013

Contents

Chapter 1	General introduction	9
Chapter 2	Mutation-driven epigenetic alterations as a defining hallmark of central cartilaginous tumours, giant cell tumour of bone and chondroblastoma	29
Chapter 3	Histone deacetylase inhibitors as a therapeutic strategy to eliminate neoplastic “stromal” cells from giant cell tumors of bone	51
Chapter 4	Beyond the influence of <i>IDH</i> mutations: Exploring epigenetic vulnerabilities in chondrosarcoma	83
Chapter 5	Inhibition of PARP sensitizes chondrosarcoma cell lines to chemo- and radiotherapy irrespective of the <i>IDH1</i> or <i>IDH2</i> mutation status	145
Chapter 6	Does PARP inhibition sensitize chondrosarcoma cell lines to chemotherapy or radiotherapy? Results from a three-dimensional spheroid cell model	173
Chapter 7	Targeting vulnerabilities in endogenous versus artificially created <i>IDH</i> mutant chondrosarcoma cell lines: The model matters	199
Chapter 8	Summary, discussion, and future perspectives	231
Appendices	Nederlandse samenvatting	249
	Curriculum Vitae	257
	List of publications	259
	Nwoord	263