

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/19755> holds various files of this Leiden University dissertation.

Author: Berghuis, Dagmar

Title: Tumor - host immune interactions in Ewing sarcoma : implications for therapy

Issue Date: 2012-09-06

**Tumor - host immune interactions
in Ewing sarcoma**

implications for therapy

Dagmar Berghuis

The work presented in this thesis was financially supported by EuroBoNeT, a European Commission granted Network of Excellence for studying the pathology and genetics of bone tumors (018814); Dutch Cancer Society Nederlandse Kankerbestrijding/ Koningin Wilhelmina Fonds (RUL 2003-2800); Stichting The Quality of Life Gala 2007

Publication of this thesis was financially supported by the Department of Pathology, Leiden University Medical Center, Leiden and Willem-Alexander Kinderziekenhuis, Leiden.

Cover art: M.M.L. (Leyla) van Esch, 2012

Lay-out and printing: Off Page (www.offpage.nl)

ISBN: 978-94-6182-143-0

Copyright 2012. Dagmar Berghuis, Voorhout. All rights reserved. No part of this publication may be reproduced in any form or by any means without prior permission of the author.

**Tumor – host immune interactions
in Ewing sarcoma**

implications for therapy

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. P.F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op donderdag 6 september 2012
klokke 13.45 uur

door

Dagmar Berghuis

geboren te Warnsveld
in 1981

Promotiecommissie

Promotores: Prof. Dr. P.C.W. Hogendoorn
Prof. Dr. R.M. Egeler

Co-promotor: Dr. A.C. Lankester

Overige leden: Prof. Dr. E. de Alava
(Centro de Investigación del Cáncer, Salamanca, Spain)

Prof. Dr. H. Gelderblom

Prof. Dr. J.B.A.G. Haanen

Prof. Dr. H. Juergens
(University Children's Hospital, Munster, Germany)

Prof. Dr. C.J.M. Melief

Voor mijn gezin

CONTENTS

Chapter 1	General introduction	9
Chapter 2	Pro-inflammatory chemokine – chemokine receptor interactions within the Ewing sarcoma microenvironment determine CD8 ⁺ T-lymphocyte infiltration and affect tumour progression <i>J Pathol 2011; 223 (3): 347</i>	31
Chapter 3	Reduced Human Leukocyte Antigen expression in advanced-stage Ewing sarcoma: implications for immune recognition <i>J Pathol 2009; 218 (2): 222</i>	59
Chapter 4	Expression of cellular FLICE inhibitory protein, caspase-8 and protease inhibitor-9 in Ewing sarcoma and implications for susceptibility to cytotoxic pathways <i>Clin Cancer Res 2007; 13 (1): 206</i>	77
Chapter 5	Histone Deacetylase Inhibitors Enhance Expression of NKG2D Ligands in Ewing Sarcoma and Sensitize for Natural Killer Cell-Mediated Cytolysis <i>Clin Sarcoma Res 2012; 2 (1): 8</i>	97
Chapter 6	The CXCR4-CXCL12 axis in Ewing sarcoma: promotion of tumor growth rather than metastatic disease <i>Submitted</i>	123
Chapter 7	Summary and future perspectives	141
Chapter 8	Nederlandse samenvatting	151
Chapter 9	Curriculum vitae	161
	List of abbreviations	163