

VU Research Portal

Design of SF3B1 subunit modulators of the SF3B spliceosome complex

Randazzo, Ornella

2022

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Randazzo, O. (2022). *Design of SF3B1 subunit modulators of the SF3B spliceosome complex*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

CONTENTS

Chapter 1	Introduction and Thesis outline	4
	1. About the pancreas: structure and function	5
	1.1 Overview of pancreatic cancer: types and focus on Pancreatic Ductal Adenocarcinoma (PDAC)	6
	1.2 Worldwide incidence of pancreatic cancer	8
	1.3 Causes and risk factors	9
	1.4 Pathogenesis of PDAC	10
	1.5 Signs and symptoms	12
	1.6 Early detection, diagnosis and staging	13
	1.7 Treatment and future perspectives	14
	2. Pre-mRNA splicing: the spliceosome and the biochemical mechanism of splicing	16
	2.1 Alternative splicing: its several patterns and regulation mechanisms	17
	2.2 SF3B complex with special focus on SF3B1	19
	2.3 Targeting splicing as potential therapeutic approach	20
	2.4 Splicing deregulation and anticancer drug resistance	23
	3. The chemistry of heterocycles as potential strategy in cancer research	24
	4. Thesis outline	26
Chapter 2	<i>“Open Sesame?”: Biomarker Status of the Human Equilibrative Nucleoside Transporter-1 and Molecular Mechanisms Influencing its Expression and Activity in the Uptake and Cytotoxicity of Gemcitabine in Pancreatic Cancer</i>	36
	Ornella Randazzo* , Filippo Papini*, Giulia Mantini, Alessandro Gregori, Barbara Parrino, Daniel S.K. Liu, Stella M. Cascioferro, Daniela Carbone, Godefridus J. Peters, Adam E. Frampton, Ingrid Garajova**, Elisa Giovannetti**	
	*These authors contributed equally	
	**These authors contributed equally	

Cancers (Basel). 2020 Oct 31;12(11):3206. doi: 10.3390/cancers12113206.

- Chapter 3** *New Imidazo[2,1-b][1,3,4]Thiadiazole Derivatives Inhibit FAK Phosphorylation and Potentiate the Antiproliferative Effects of Gemcitabine Through Modulation of the Human Equilibrative Nucleoside Transporter-1 in Peritoneal Mesothelioma* 74

Giovanna Li Petri*, Camilla Pecoraro*, **Ornella Randazzo***, Silvia Zoppi, Stella M. Cascioferro, Barbara Parrino, Daniela Carbone, Btissame El Hassouni, Andrea Cavazzoni, Nadia Zaffaroni, Girolamo Cirrincione, Patrizia Diana, Godefridus J. Peters, Elisa Giovannetti

*These authors contributed equally

Anticancer Res. 2020 Sep;40(9):4913-4919. doi: 10.21873/anticancerres.14494.

- Chapter 4** *Interrelationship between miRNA and splicing factors in pancreatic ductal adenocarcinoma* 88

I Gede Putu Supadmanaba*, Giulia Mantini*, **Ornella Randazzo***, Mjriam Capula, Ittai B. Muller, Stella M. Cascioferro, Patrizia Diana, Godefridus J. Peters, Elisa Giovannetti

*These authors contributed equally

Epigenetics. 2021 May 30;1-24. doi: 10.1080/15592294.2021.1916697.

- Chapter 5** *Exploring splicing modulation as a novel strategy against pancreatic cancer* 135

Rocco Sciarrillo*, **Ornella Randazzo***, Giulia Mantini*, Btissame El Hassouni, I Gede Putu Supadmanaba, Tonny Lagerweij, Tom Würdinger, Godefridus J. Peters, Carla F.M. Molthoff, Gerrit Jansen, Gertjan J.L. Kaspers, Jacqueline Cloos, Elisa Giovannetti

*These authors contributed equally

Manuscript in preparation

Chapter 6	<i>SF3B1 modulators affect key genes in metastasis and drug influx: a new approach to fight pancreatic cancer chemoresistance</i>	162
	Ornella Randazzo* , Stella M. Cascioferro*, Camilla Pecoraro*, Widad Ait Iddouch, Amir Avan, Barbara Parrino, Daniela Carbone, Ugo Perricone, Godefridus J. Peters, Patrizia Diana, Elisa Giovannetti	
	*These authors contributed equally	
	Cancer Drug Resist 2021;4:904-922. doi: 10.20517/cdr.2021.61.	
Chapter 7	Discussion and conclusions	192
Chapter 8	English summary Riassunto in Italiano Samenvatting	203
Appendices	<i>Curriculum vitae</i> List of publications Acknowledgements	211