

VU Research Portal

Interplay between phase I and phase II biotransformation of drugs

Vredenburg, G.

2015

document version

Publisher's PDF, also known as Version of record

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

citation for published version (APA)

Vredenburg, G. (2015). *Interplay between phase I and phase II biotransformation of drugs: In vitro approaches to study the formation and fate of reactive metabolites.*

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

PART I	INTRODUCTION	
Chapter 1	General introduction	9
PART II	YEAST AS A CELLULAR MODEL TO STUDY DRUG METABOLISM AND METABOLISM-RELATED TOXICITY	
Chapter 2	Metabolism related toxicity of diclofenac in yeast as model system	41
Chapter 3	Reconstitution of the interplay between cytochrome P450s and human glutathione S-transferases in clozapine metabolism in yeast	57
PART III	FORMATION AND DETOXIFICATION OF (REACTIVE) DRUG METABOLITES USING RECOMBINANT ENZYMES	
Chapter 4	Human NAD(P)H:quinone oxidoreductase 1 (NQO1)-mediated inactivation of reactive quinoneimine metabolites of diclofenac and mefenamic acid	79
Chapter 5	Activation of the anticancer drugs cyclophosphamide and ifosfamide by cytochrome P450 BM3 mutants	101
Chapter 6	Selective whole-cell biosynthesis of the designer drug metabolites 15- or 16- β -hydroxynorethisterone by engineered cytochrome P450 BM3 mutants	121
PART IV	CONCLUSIONS	
Chapter 7	Summary, conclusions and perspectives	153
Appendices:	Nederlandse samenvatting	166
	List of publications	170
	Curriculum Vitae	171
	Dankwoord	172