



The complex inositol metabolism of *Corynebacterium glutamicum* and its application for the production of rare inositols

Paul Ramp

Schlüsseltechnologien / Key Technologies
Band / Volume 269
ISBN 978-3-95806-699-1

Forschungszentrum Jülich GmbH
Institut für Bio- und Geowissenschaften
Biotechnologie (IBG-1)

**The complex inositol metabolism
of *Corynebacterium glutamicum*
and its application for the production
of rare inositols**

Paul Ramp

Schriften des Forschungszentrums Jülich
Reihe Schlüsseltechnologien / Key Technologies

Band / Volume 269

ISSN 1866-1807

ISBN 978-3-95806-699-1

Content

Summary	III
Zusammenfassung.....	IV
Abbreviations.....	V
1. Introduction.....	1
1.1 Inositol isomers and derivatives	1
1.2 Inositols in human metabolism and their pharmaceutical relevance	4
1.2.1 Role in insulin signaling and treatment of insulin resistance.....	7
1.2.2 Role in treatment of Alzheimer's disease	9
1.3 Bacterial inositol metabolism	11
1.3.1 Inositol catabolism	11
1.3.2 Role of inositols in <i>Actinobacteria</i>	15
1.3.3 Features of <i>Corynebacterium glutamicum</i>	16
1.3.4 Inositol metabolism and its regulation in <i>C. glutamicum</i>	17
1.4 Inositol market and production.....	19
1.4.1 Conventional production	20
1.4.2 Biotechnological production of inositols	21
1.5 Aims of this thesis	23
2. Results	24
2.1 Metabolic engineering of <i>Corynebacterium glutamicum</i> for production of <i>scyllo</i> -inositol, a drug candidate against Alzheimer's disease.....	26
2.2 Physiological, biochemical, and structural bioinformatics analysis of the multiple inositol dehydrogenases from <i>Corynebacterium glutamicum</i>	41
2.3 Production of D- <i>chiro</i> -inositol with <i>Corynebacterium glutamicum</i> via two different synthesis routes	78
2.3.1 Abstract	80
2.3.2 Introduction	80
2.3.3 Materials and Methods	82
2.3.4 Results and Discussion.....	87
2.3.5 Conclusion and Outlook.....	98
2.3.6 Acknowledgements	99
2.3.7 References	100
3. Discussion.....	106
3.1 The complexity of the <i>C. glutamicum</i> inositol catabolism.....	106
3.2 Making sense of multiple inositol dehydrogenase activities	107

Content

3.3	Inosose isomerases – The missing link?.....	111
3.4	Regulation of the inositol metabolism in <i>C. glutamicum</i>	114
3.5	<i>C. glutamicum</i> as a suitable host for production of rare inositols	116
3.6	Novel synthesis routes and prospects for the production of other inositols	120
3.7	Conclusion.....	123
4.	References.....	126
5.	Appendix.....	144
5.1	L-chiro-inositol metabolism in <i>C. glutamicum</i>	144
5.1.1	Background	144
5.1.2	Results and Discussion.....	144
5.2	Structure elucidation of the scyllo-inositol dehydrogenase IolW	147
5.2.1	Background	147
5.2.2	Experimental setup	148
5.2.3	Results and Discussion.....	151
5.3	References Appendix.....	158
6.	Acknowledgement	159
7.	Erklärung.....	161

Schlüsseltechnologien / Key Technologies
Band / Volume 269
ISBN 978-3-95806-699-1