

University of Groningen

## That gut instinct! Novel insights in the interplay between the microbiota, serotonin metabolism and gut function

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*That gut instinct!*

**Novel insights in the interplay between the  
microbiota, serotonin metabolism and gut  
function**

**Barbora Waclawiková**



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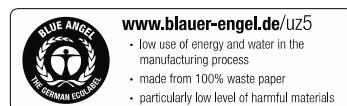
faculty of science  
 and engineering

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university of  
groningen

***That gut instinct!***  
**Novel insights in the interplay between the  
microbiota, serotonin metabolism and gut  
function**

**PhD thesis**

to obtain the degree of PhD at the  
University of Groningen  
on the authority of the  
Rector Magnificus prof. dr. C. Wijmenga  
and in accordance with the decision by the College of Deans.

This thesis will be defended in public on

Tuesday 7 June 2022 at 16.15 hours

by

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## **Brief Summary**

The gut microbiota-derived metabolites are evident to have a substantial effect on the regulation of various host functions. Despite the vast number of studies dissecting the host-microbiota interactions over the last years, enormous efforts are still needed to fully unravel the underlying mechanisms of this crosstalk, thereby potentiating the application of microbiota-targeted therapies in clinical practice and in a personalized manner.

This thesis investigates the interplay between the microbiota, serotonin metabolism, and gut function. We showed that a wide range of gut microbiota can convert, the serotonin precursor, 5-hydroxytryptophan into an indole derivative. This bacterial product showed a potent stimulatory effect on the intestinal motility via activation of calcium channels, and a marginal effect on the microbiota composition. Besides, we uncovered the bacterial metabolization of serotonin and how this process impacts both the bacteria and its host. The outcome of this thesis has brought new insight in the physiological role of bacteria-derived indoles and may help the design of novel microbiota-based therapeutics targeting gut motility.



## **Beknopte Samenvatting**

Het is duidelijk dat de microbiële metabolieten in de darm een substantieel effect hebben op de regulatie van verschillende gastheerfuncties. Ondanks het enorme aantal onderzoeken dat de afgelopen jaren de interacties tussen gastheer en microbiota probeert te ontrafelen, zijn er nog steeds enorme inspanningen nodig om de onderliggende mechanismen van deze samenspraak volledig te begrijpen zodat de toepassing van op microbiota gerichte therapieën in de klinische praktijk en op een gepersonaliseerde manier mogelijk wordt gemaakt.

Dit proefschrift onderzoekt de wisselwerking tussen de microbiota, het serotoninemetabolisme en de darmfunctie. We toonden aan dat een breed scala van darmmicrobiota de serotoninevoorloper, 5-hydroxytryptofaan, kan omzetten in een indoolderivaat. Dit bacteriële product vertoonde een krachtig stimulerend effect op de darmmotiliteit via activering van calciumkanalen en een marginaal effect op de microbiota-samenstelling. Bovendien hebben we de bacteriële metabolisatie van serotonine opgehelderd, alsmede hoe dit proces zowel de bacteriën als de gastheer beïnvloedt. De uitkomst van dit proefschrift heeft nieuw inzicht gegeven in de fysiologische rol van de van bacteriën afgeleide indolen en kan helpen bij het ontwerpen van nieuwe, op microbiota gebaseerde therapieën, die gericht zijn op darmmotiliteit.





# TABLE OF CONTENTS

<b>CHAPTER 1 .....</b>	<b>13</b>
Introduction	14
<b>CHAPTER 2 .....</b>	<b>45</b>
Gut bacteria-derived 5-hydroxyindole is a potent stimulant of intestinal motility via its action on L-type calcium channels	46
<b>CHAPTER 3 .....</b>	<b>97</b>
Oral administration of the gut-bacterial metabolite 5-hydroxyindole and its subsequent acceleration of gut motility have marginal effects on the rat microbiota	98
<b>CHAPTER 4 .....</b>	<b>113</b>
Deciphering the potency of 5-hydroxyindole stimulatory effect on the rat colonic smooth muscles and its binding sites on the L-type voltage-gated calcium channels	114
<b>CHAPTER 5 .....</b>	<b>139</b>
Serotonin degradation possibly protects <i>Pseudomonas fluorescens</i> from oxidative stress and enhances intestinal epithelial barrier function	140
<b>CHAPTER 6 .....</b>	<b>177</b>
General discussion, future perspectives and concluding remarks	178
<b>APPENDIX.....</b>	<b>195</b>
Public summary	196
Samenvatting voor het brede publiek	198
Shrnutí	200
Acknowledgments	202
About the author	214
List of publications	216



