

Résumé Non Technique (RNT)

Titre du projet de recherche (Doit être identique au titre dans la demande de projet)	Immune response changes in a dietary fiber-induced colonic mucus degradation that lead to a higher pathogen susceptibility	
But du projet de recherche (Cochez la case correspondante, des sélections multiples sont possibles)	Recherche fondamentale Recherche translationnelle et appliquée Application pour des fins réglementaires et la production de routine Protection de l'environnement dans l'intérêt de la santé et du bien-être des hommes et des animaux Préservation des espèces Formation supérieure ou formation ayant le but d'obtenir, de préserver et de développer des capacités professionnelles Examens forensiques / Requêtes légales Conservation des colonies d'animaux génétiquement modifiés, qui ne sont pas utilisés dans d'autres projets de recherche	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Bénéfices prévus à travers ce projet de recherche (max. 1500 caractères) Quelles sont les avancées scientifiques qui pourront être tirées de ce projet (concernant l'homme et les animaux) ?	Dysbiosis of the intestinal microbiota can have severe consequences and it is thought that a disturbance of the microbial community might be the cause of diseases such as inflammatory bowel diseases (IBD). Little is known about the mechanisms of how a disturbance of the microbial community occurs and which possible impact this can have on the immune response. We have recently investigated the effects of a fiber-free diet (FF) in a gnotobiotic mouse model (wild-type Swiss Webster) in a 14 member synthetic microbial community (SM) showing that mucus-degrading bacteria outcompete fiber-degrading bacteria causing a degradation of the mucus layer in the colon. Furthermore, the microbial community deprived of dietary-fiber showed a higher susceptibility to an infection with <i>C. rodentium</i>	

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	<p>(Desai et al. <i>Cell</i>, 2016, 167:1339-1353). Another recent experiment with SM in C57BL/6 mice (unpublished data) has shown that mucus-degrading bacteria are necessary to enhance <i>C. rodentium</i> susceptibility in the model used in the Cell paper. Thus there must be underlying changes in the immune cells caused by the mucus degradation that enhances <i>C. rodentium</i> susceptibility. <i>C. rodentium</i> is a gram-negative enteric mouse pathogen equivalent of the human pathogenic EPEC (<i>Enteropathogenic Escherichia coli</i>) which has to traverse the mucus barrier to infect the host.</p> <p>This project therefore aims to investigate the underlying changes in the immune response caused by mucus-degrading bacteria that leads to a higher <i>C. rodentium</i> susceptibility in a complex microbial community (SPF mice).</p>		
<p>Dommages causés à travers ce projet de recherche (max. 500 caractères) Quels sont les éventuels effets néfastes attendus sur les animaux ? Qu'arrive-t-il aux animaux à la fin de l'expérience ? Nommez le niveau de sévérité selon le Chapitre III, article 15, 1. de la Directive européenne 2010/63/UE.</p>	<p>The infection with <i>C. rodentium</i> can cause weight loss of the animals with be monitored daily for three weeks after the infection. Animals that lose more than 20% of weight will be excluded from the study and euthanized. If the animals show furthermore any sign of rectal prolapse or loss of activity (hunched position) they will be euthanized.</p>		
<p>Espèce et nombre d'animaux utilisés Cochez la case correspondante et indiquez le nombre. Des sélections multiples sont possibles.</p>	<p>Souris</p> <p>Rats</p> <p>Poissons zébra</p> <p>Autres</p>	<p><input checked="" type="checkbox"/></p> <p><input type="checkbox"/></p> <p><input type="checkbox"/></p> <p><input type="checkbox"/></p>	<p>n= 80</p> <p>n=</p> <p>n=</p> <p>n=</p>
<p>Application du principe des 3 R de Russel et Burch (1959) (Laissez-vous guider par les questions)</p>			
<p>Remplacement / Remplacement (max. 500 caractères) Pourquoi le but de ce projet ne peut-il être atteint par d'autres méthodes ? Pourquoi l'expérimentation animale ne peut-elle être remplacée ?</p>	<p>We aim to investigate the underlying changes in the immune response caused by mucus degradation that lead to a higher pathogen susceptibility of <i>C. rodentium</i>. These experiments intend to assess complex physiologic interactions for which a functioning and complete organism is essential. Alternative approaches to the animal use are thus not possible. The interplay of diet, microbial community abundance and <i>C. rodentium</i> infection</p>		

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	will be evaluated. The phenotype of a thin and a thick mucus layer will be created which is only possible in vivo by using a fiber-free and a fiber-rich diet. In addition, an infection with <i>C. rodentium</i> will be induced to investigate the question why mucus degradation leads to a higher pathogen susceptibility.
Reduction / Réduction (max. 500 caractères) Expliquer comment le nombre d'animaux utilisé est réduit au minimum indispensable (biostatistiques) ?	We have chosen to use C57BL/6 mice for our experiments because this species is known to be a well-developed model for the investigation of the human immune system. In regards to the animal numbers, we have determined 40 animals per group (80 in total) to be statistically significant. This number of animals is needed for the readouts such as RNA extraction, mucus layer measurements, fecal and cecal bacterial community analyses, cecal enzyme assays, etc. It is known that some mice could have to be euthanized with regard to the human end point due to the development of colitis and a weight loss higher than 20%.
Refinement /Amélioration (max. 500 caractères) Expliquer les mesures générales mises en œuvre pour minimiser les répercussions négatives sur le bien-être animal? Comment les dommages sont-ils réduits ? Pourquoi utilisez-vous cette espèce précise ?	Occurring symptoms during an infection with <i>C. rodentium</i> are generally considered as very mild. Beside diarrhea and weight loss, the animals will develop characteristic colitis. Due to this symptoms it is important to avoid dehydration, which is why water will be permanently offered to the animals. In case of dehydration, mice will be rehydrated with an isotonic 0.9% NaCl solution (ip injection).

