Summary

In one aspect, the present disclosure refers to the use of fecal matter in the manufacture of a medicament for the prevention or treatment of an autoimmune disease, wherein the fecal matter which is autologous to a subject is to be administered to the subject, wherein the autoimmune disease is not inflammatory bowel syndrome (IBD), and wherein, if the use is for treatment of autoimmune disease, the fecal matter is obtained from the subject while having the autoimmune disease.

The present inventors investigated whether administration of fecal transplants, from either allogenic (healthy donor) or autologous (own) sources, may have beneficial effects in patients with autoimmune disease.

Surprisingly, the present inventors found that administration of autologous fecal transplants can bring about an immune reset within patients with autoimmune disease.

Without being bound by any theory, the present inventors consider that the autologous fecal matter may modulate the immune system, e.g. by resetting B-cell clone function and regulatory T-cells, which in turn may inhibit autoimmune response.

It is thought that during early life, the immune system is trained via continuous crosstalk with a developing intestinal microbiome composition. In this way, the intestinal microbiome plays an essential role in modulating adaptive immune cell development, composition, and function (see e.g. Agace and McCoy Immunity 46, April 18, 2017). It is this process, amongst others, that leads to a proper functioning immune system, devoid of autoimmune factors.

However, the crosstalk between the immune system and the intestinal microbiome, or the end result thereof, may be disturbed, which can lead to the production of autoimmune antibodies. The treatment according to the present disclosure may overcome this disturbance, by re-initiating the crosstalk between the immune system and the intestinal microbiome (including its specific bacteria, viruses, fungi and/or derived products such as metabolites or microbial cell envelope compounds, as well as miRNA).

Accordingly, the use of autologous fecal matter (such as autologous fecal microbiota transplants) in autoimmune diseases, may stop the autoimmune destruction of targeted tissue and re-establish immune tolerance. The present disclosure can achieve this by stimulating the immune system, wherein the autologous fecal matter is preferably administered to the duodenum (directly or indirectly such as via oral administration). The present disclosure preferably does not aim to alter the intestinal microbiome, i.e. the gut microbiota composition.

Hence, the present disclosure is aimed at the treatment of autoimmune diseases, particularly endocrine autoimmune diseases (e.g. Type 1 Diabetes mellitus, Hashimoto's hypothyreoidism disease, Graves's hyperthyreoidism disease, and Addison's disease), Vitiligo, Celiac disease, Psoriasis (arthritis), rheumatoid arthritis, and/or Bechterew's disease. Also, prevention and/or treatment of asthma is encompassed, which may be explained by the

Claims

1. Use of fecal matter in the manufacture of a medicament for the prevention or treatment of an autoimmune disease, wherein the fecal matter which is autologous to a subject is to be administered to the subject, wherein the autoimmune disease is not inflammatory bowel syndrome (IBD), and wherein, if the use is for treatment of autoimmune disease, the fecal matter is obtained from the subject while having the autoimmune disease.

2. The use according to claim 1, wherein the autoimmune disease is chosen from the group consisting of Type 1 Diabetes mellitus, thyroid autoimmune disease, Addison's disease, Psoriasis, Vitiligo, rheumatoid autoimmune disease, Celiac disease, Asthma, and Addison's disease.

3. The use according to claim 2, wherein the thyroid autoimmune disease is chosen from the group consisting of Hashimoto's disease, and Graves' disease.

4. The use according to claim 2, wherein the rheumatoid disorder is chosen from the group consisting of Rheumatoid arthritis and Bechterew's disease.

5. The use according to claim 2, wherein the psoriaris is accompanied with psoriatic arthritis.

6. The use according to any one of the previous claims, wherein the fecal matter is to be administered to the small intestine, preferably the duodenum, of the subject.

7. The use according to any one of the previous claims, wherein the fecal matter is feces or part thereof, preferably a purified part thereof.

8. The use according to any one of the previous claims, wherein the fecal matter is one or more constituents of feces, wherein said constituents are preferably chosen from the group consisting of bacteria, archaea, viruses, bacteriophages, fungi, metabolites, proteins, peptides, enzymes, antibodies, antigens, toll-like receptor ligands, immune signalling components, neural signalling components and/or entero-endocrine signalling components.

9. The use according to any one of the previous claims, wherein the fecal matter is comprised in liquid medium and/or does not comprise solids having a diameter of more than

10, 25, 50, 75, 100, 200, 400, 600, 800, or 1000 µm, preferably obtained by mixing autologous feces with aqueous medium and subsequent filtering and/or centrifugation.

10. The use according to any one of the previous claims, wherein the fecal matter is combined with a tumor necrosis factor alpha (TNFα) inhibitor, preferably chosen from the group consisting of infliximab, adalimumab, certolizumab pegol, and golimumab.

11. The use according to any one of the previous claims, wherein the fecal matter is combined with bacteria from the genus *Eubacterium, Intestinimonas, Bifidobacteria, Lactobacillales* and/or *Akkermansia*, preferably chosen from the group consisting of *Bifidobacterium animalis sub lactis or Bifidobacterium breve, Lactobacillus plantarum. Lactobacillus rhamnosus, Lactobacillus acidophilus, Eubacterium hallii*, *Intestinimonas butyriciproducens,* and/or *Akkermansia muciniphila.*

12. The use according to any one of the previous claims, wherein the fecal matter is comprised in a composition, preferably a pharmaceutical composition, more preferably a liquid or solid dosage form, most preferably a capsule, a tablet, or a powder.

13. The use according to any one of the previous claims, wherein the fecal matter is comprised in and/or encapsulated by an enteric coating, preferable wherein said enteric coating does not dissolute and/or disintegrate in the gastric environment of the subject.

14. The use according to any one of the previous claims, wherein the fecal matter is present in lyophilized and/or microencapsulated form.

15. The use according to any one of the previous claims, wherein the fecal matter obtained from the subject is to be administered to the small intestine, preferably the duodenum, of said subject.

16. The use according to any one of the previous claims, wherein at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 separate administrations of fecal matter obtained from the subject is to be administered to the small intestine, preferably the duodenum, of said subject, preferably with intervals of at least 1, 2, 3, 4, 5, 6, 7, 8 weeks between said separate administrations.

17. The use according to any one of the previous claims, wherein the fecal matter is to be administered by enteral, preferably by oral, nasal or rectal administration, and/or by nasoduodenal tube administration.

18. The use according to any one of the previous claims, wherein the subject is a mammal, preferably a human.