

Patient-Derived Intestinal Organoids for Diagnosis and Drug Screening of Celiac Disease

Patients with celiac disease have a pathological reaction to gluten and have either HLA-DQ2+ (90%) or HLA-DQ8+, but expression of these MHC class II haplotypes is not sufficient and other factors are necessary for the development of celiac sprue. Diagnosis of celiac disease is determined by presence of transglutaminase 2 (TG2) autoantibody and histology of intestinal biopsies. However, those seeking diagnosis often already maintain a gluten-free diet prior to gastroenterology consultation and therefore test negative for autoantibody and present normal duodenal mucosa. So, it is necessary to have patients receive a gluten-rich diet for weeks to obtain a definitive diagnosis. Celiac patients will thus experience symptoms including diarrhea, bloating, and abdominal pain. Air-liquid interface (ALI) organoids enable culturing epithelium and stroma to recapitulate the human small intestine, and patient-derived organoids can be used for suspected celiac patient diagnosis instead. ALI organoids could be used whether the individual is on a gluten-free diet or gluten-rich diet. Specifically, ALI organoids will be challenged with gliadin and examined for gliadin presentation, immune cell expansion and activation, and epithelial cell death. It could also be used to screen the potency of drug candidates by evaluating the reduction of gliadin-dependent immune cell activation or expansion and epithelial cell death.

Applications

- Diagnosis of celiac disease using patient-derived organoids of the small intestine
- Monitoring the development of celiac disease with a precision medicine approach
- Drug discovery of therapeutic compounds for celiac disease

Advantages

- Current diagnosis relies on patients to ingest gluten, thereby inducing symptoms
 - Standard of care requires multiple analytic approaches that take weeks
 - ALI-based diagnosis enables less invasive, more efficient procedures
- Screening of drug candidates by measuring immune cell expansion and activation, and epithelial cell death

Publications

- Santos, A.J.M., van Unen, V., Lin, Z. et al. [A human autoimmune organoid model reveals IL-7 function in coeliac disease.](https://doi.org/10.1038/s41586-024-07716-2) *Nature* (2024).
<https://doi.org/10.1038/s41586-024-07716-2>
- Conger, Krista. [Organoids mimicking celiac disease show new link between gluten, intestinal damage.](#) *Stanford Medicine News Center* July 2024

Patents

- Published Application: [WO2020247528](#)
- Published Application: [20220221445](#)

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