Preterm intestinal organoids as a replacement model for necrotizing enterocolitis research

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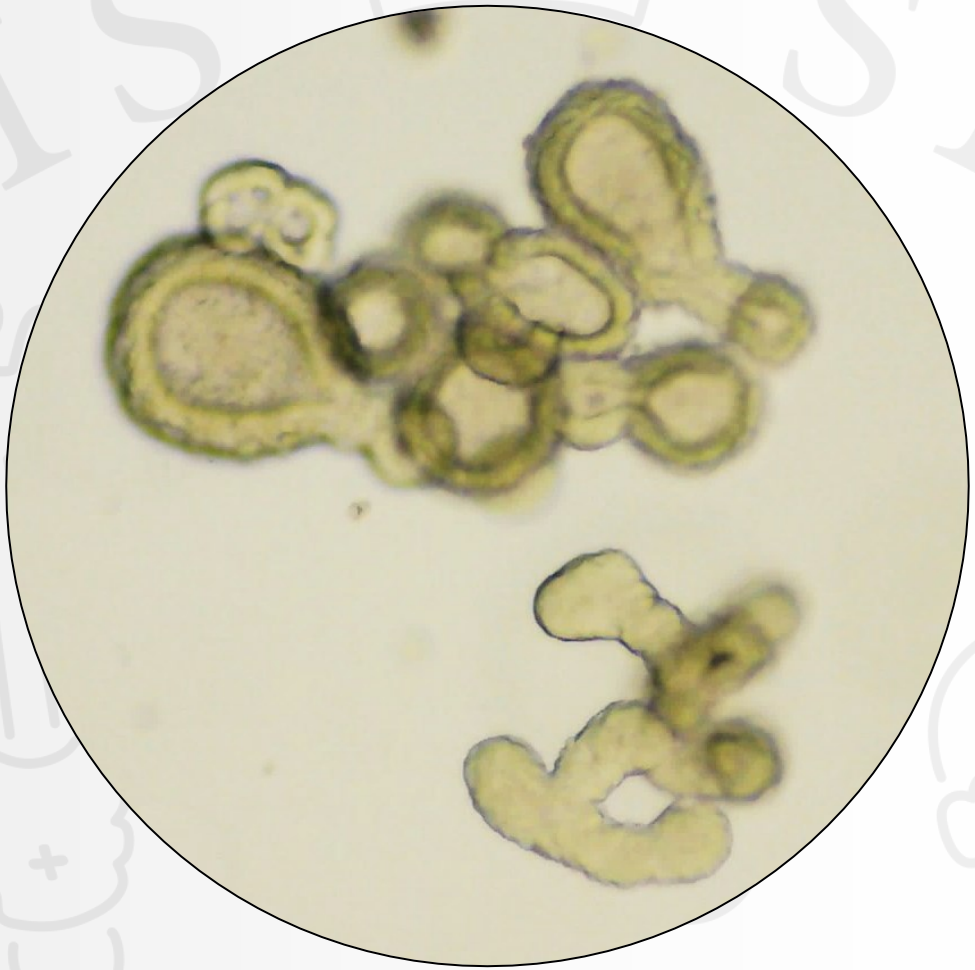


Necrotizing enterocolitis research from a 3R perspective

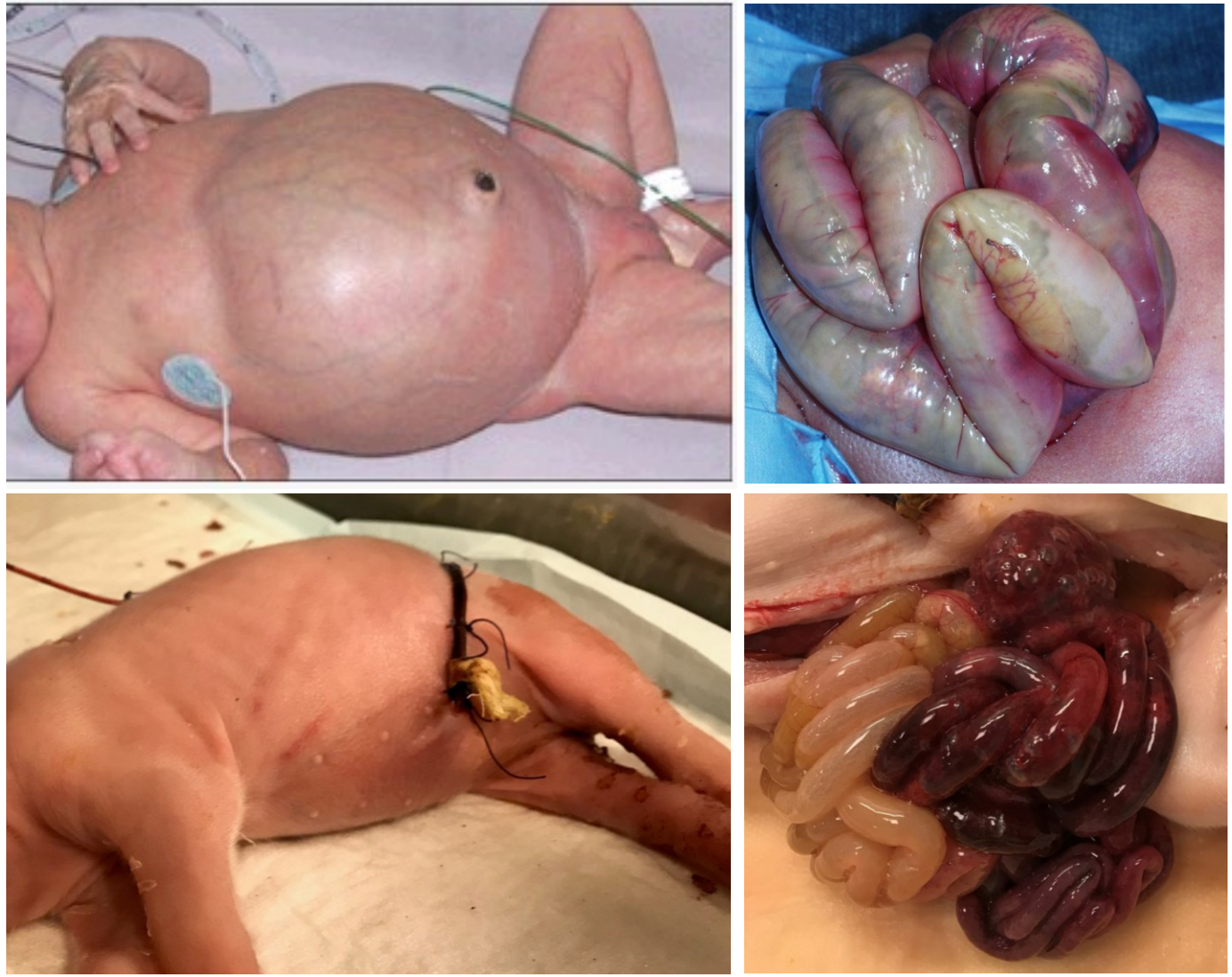
Necrotizing enterocolitis (NEC) is among the scariest emergencies in human medicine and afflicts the most vulnerable patients of all

Research is absolutely necessary, and the ambition is to eradicate NEC

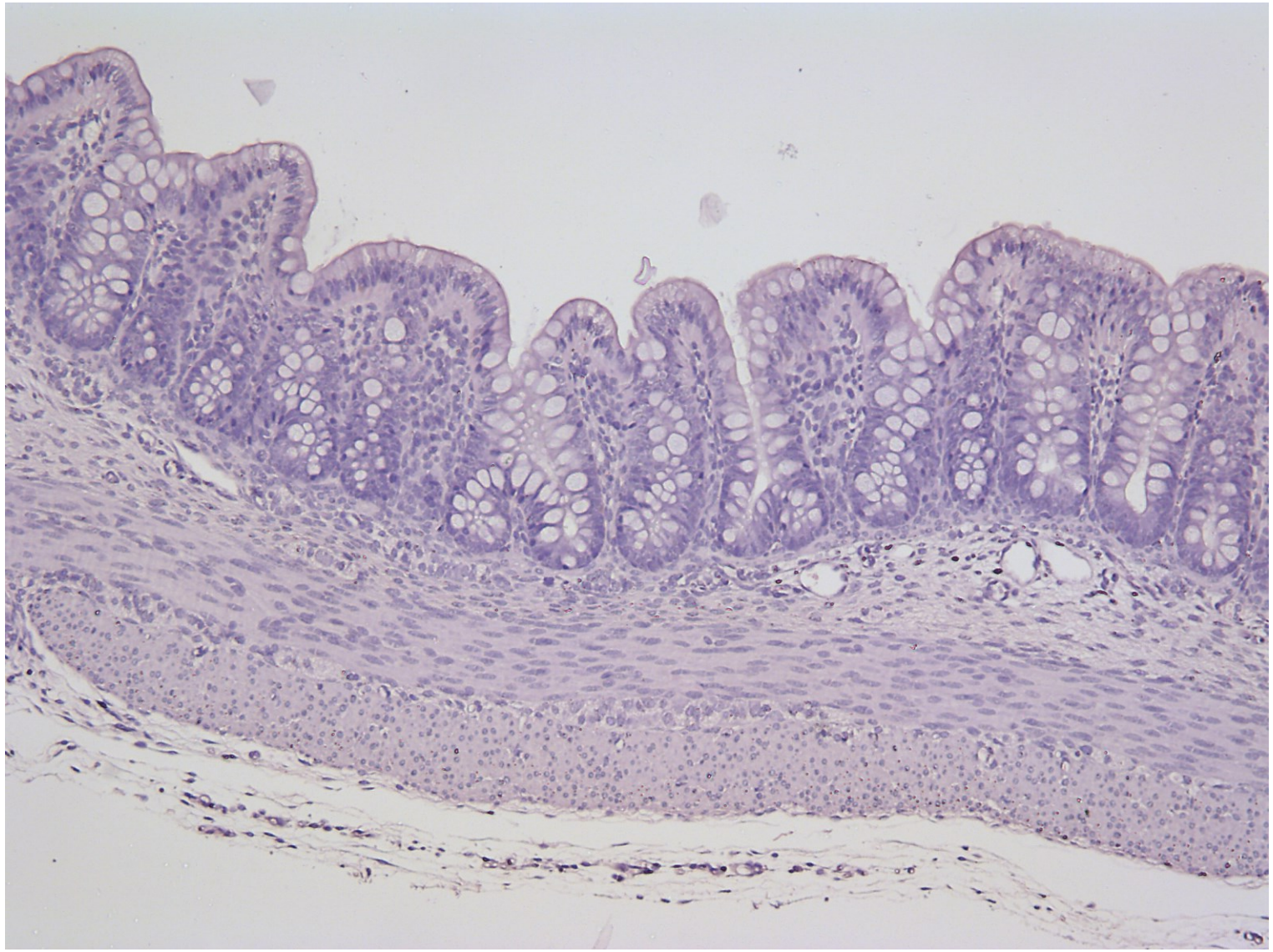
Animal models are essential for this purpose

Suffering for the animal is unavoidable

Any worthy alternative methods to replace live animals in NEC research?



NEC under the microscope: A motion picture of disaster



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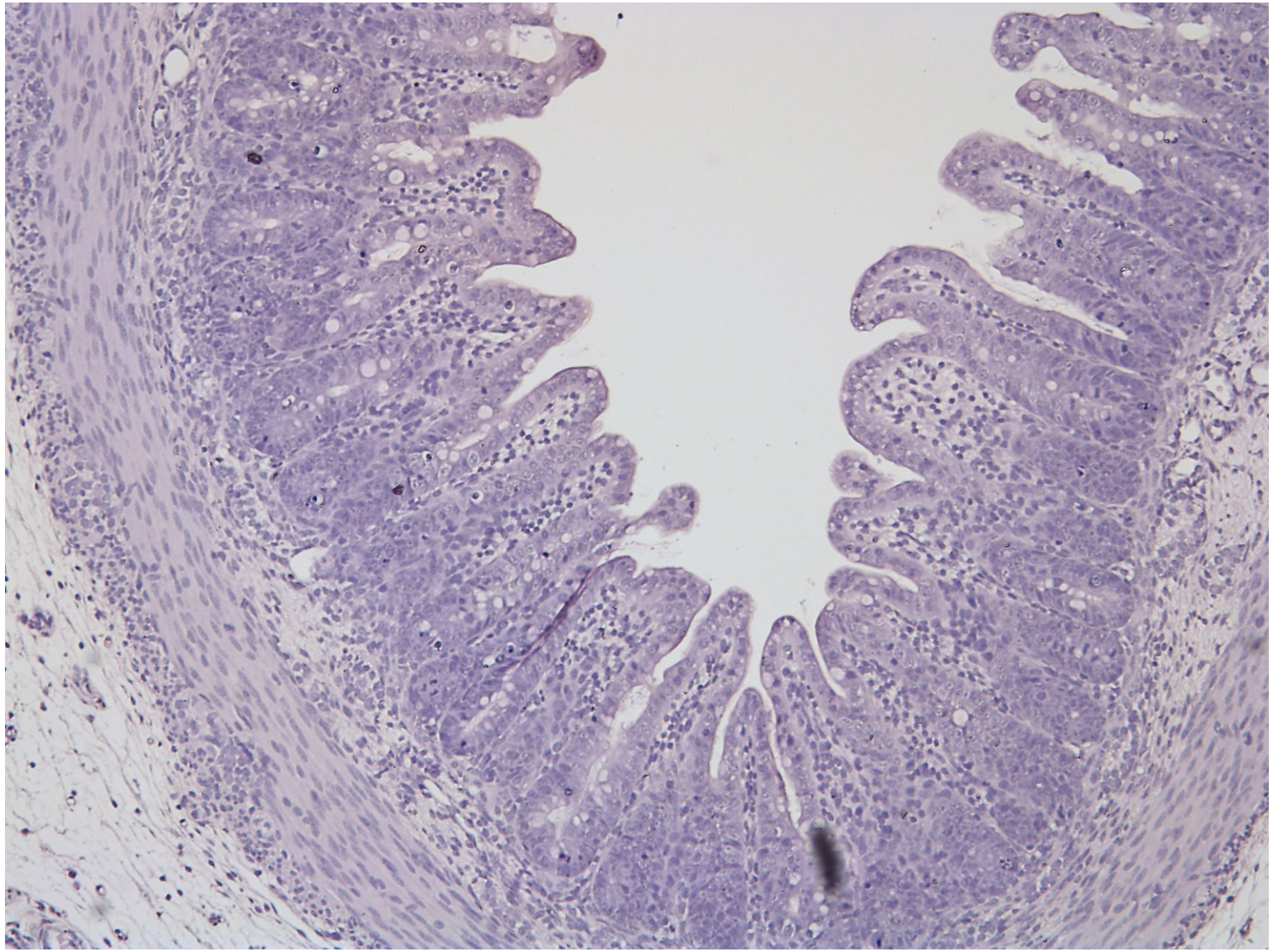

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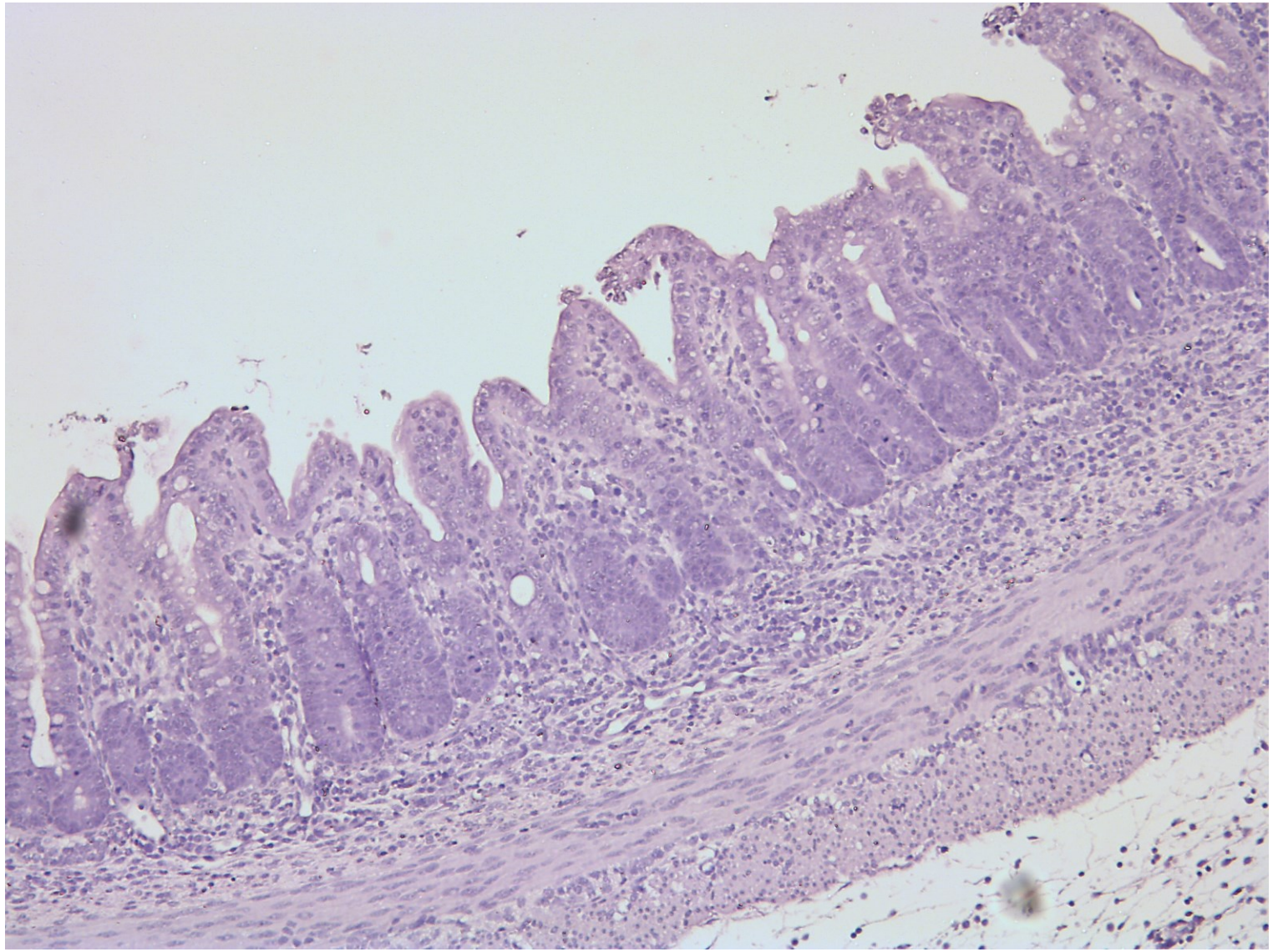

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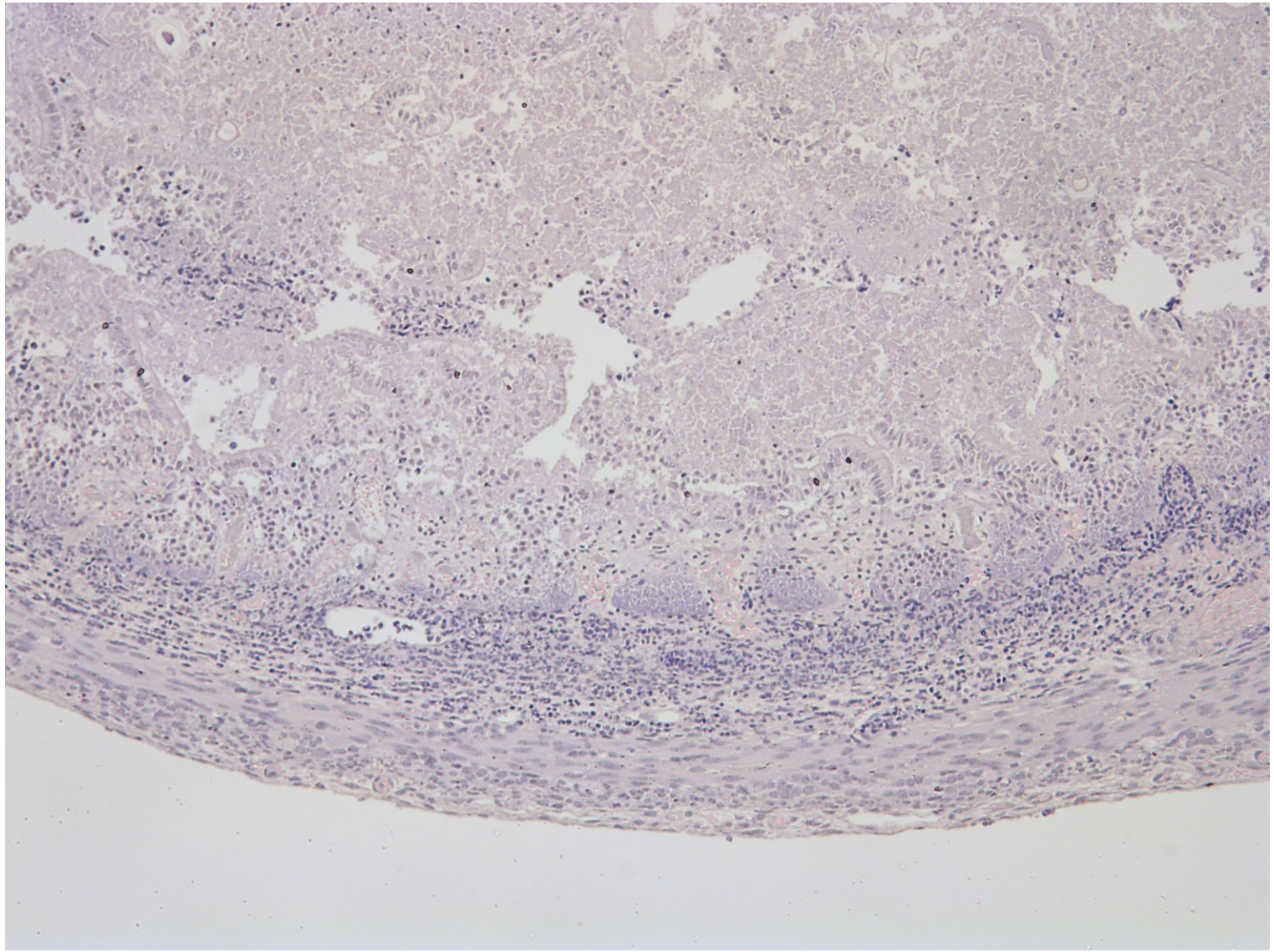

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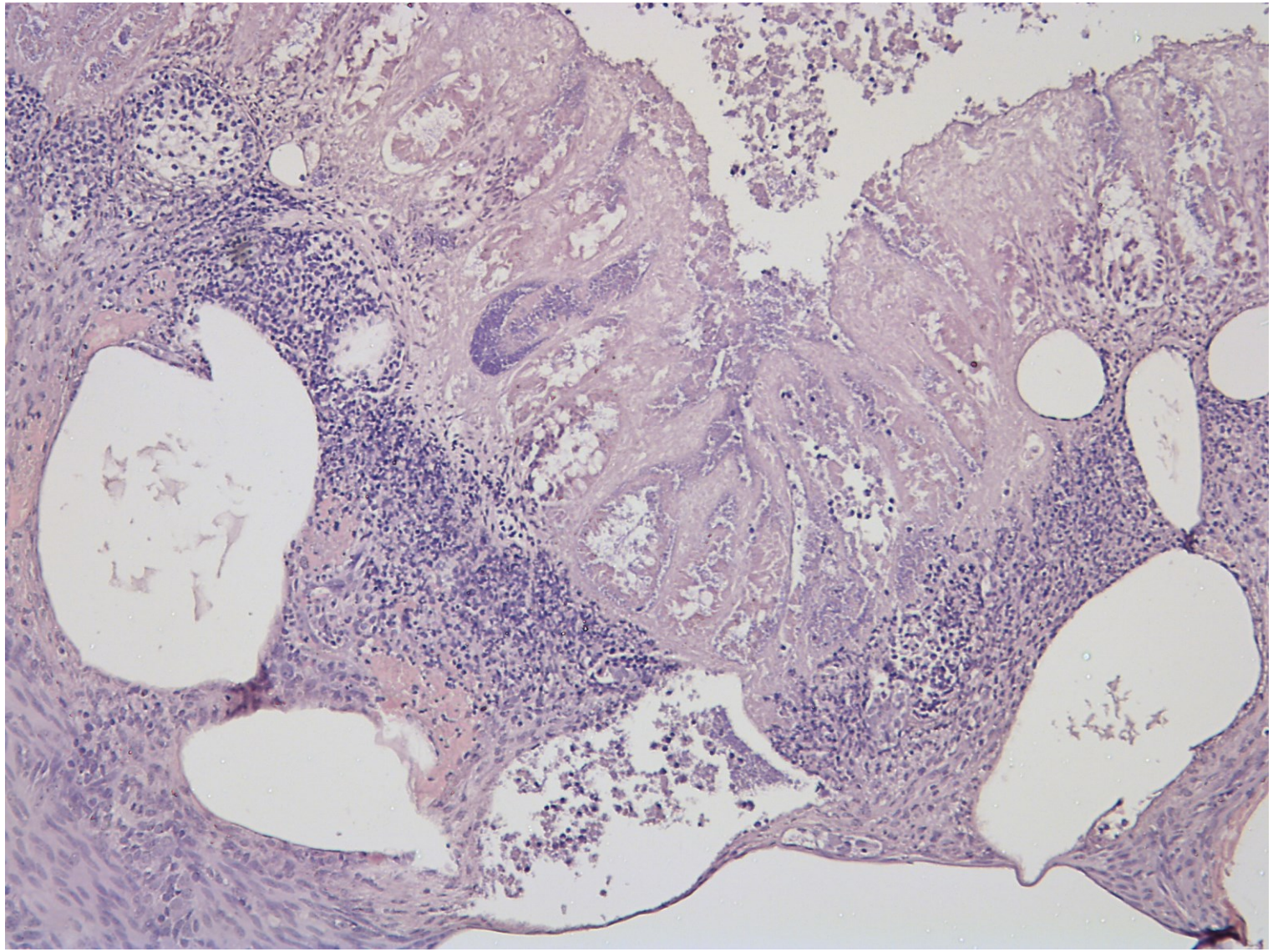


NEC under the microscope: A motion picture of disaster

What was important to notice from the "motion picture" was that the first disruptions occurred at the epithelial lining (**goblet cells** + **epithelial tips**)

If NEC is the ultimate clinical manifestation of what began as an epithelial barrier disruption ...

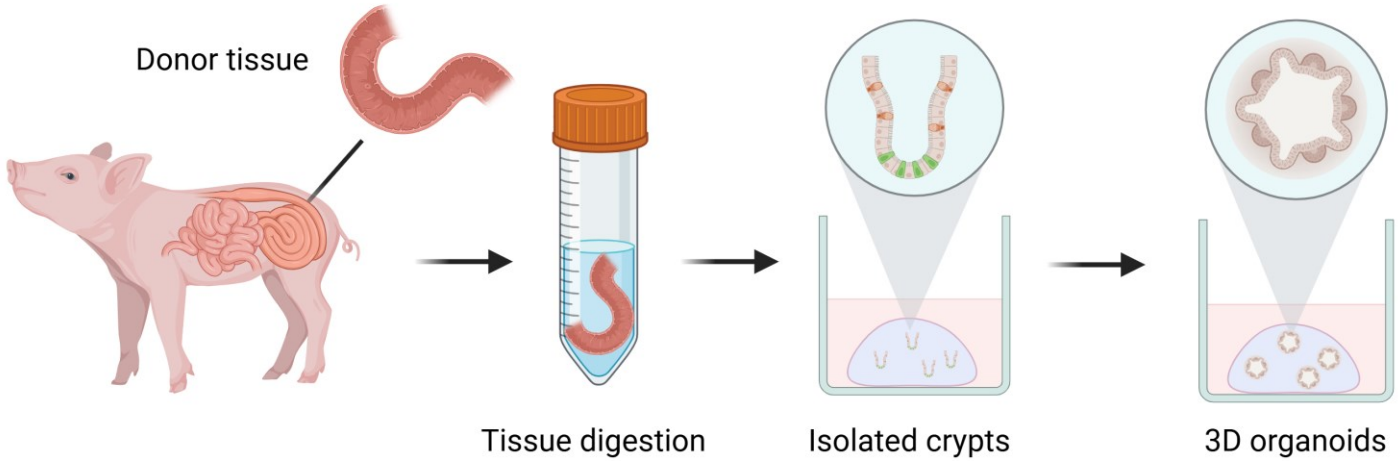
... then an *in vitro* model of the gut epithelial lining could be relevant for studying aspects of NEC including

1) mucus layer structure/function and
2) barrier integrity of the epithelial lining

Objectives of the research project

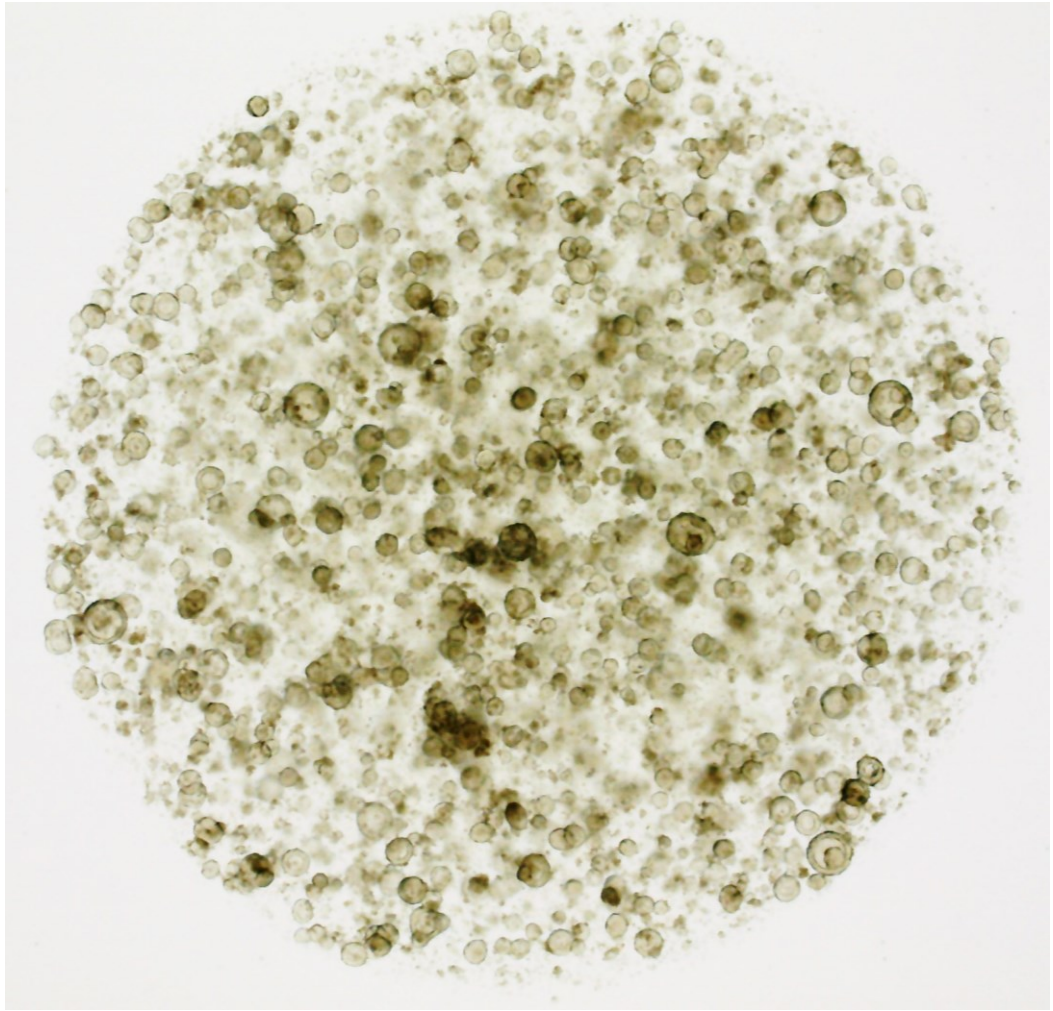
1. Culturing intestinal stem cells from preterm piglets
2. Investigating the impact of gestational age on the property of the organoid
3. Transforming spheric organoids to confluent monolayers with barrier properties

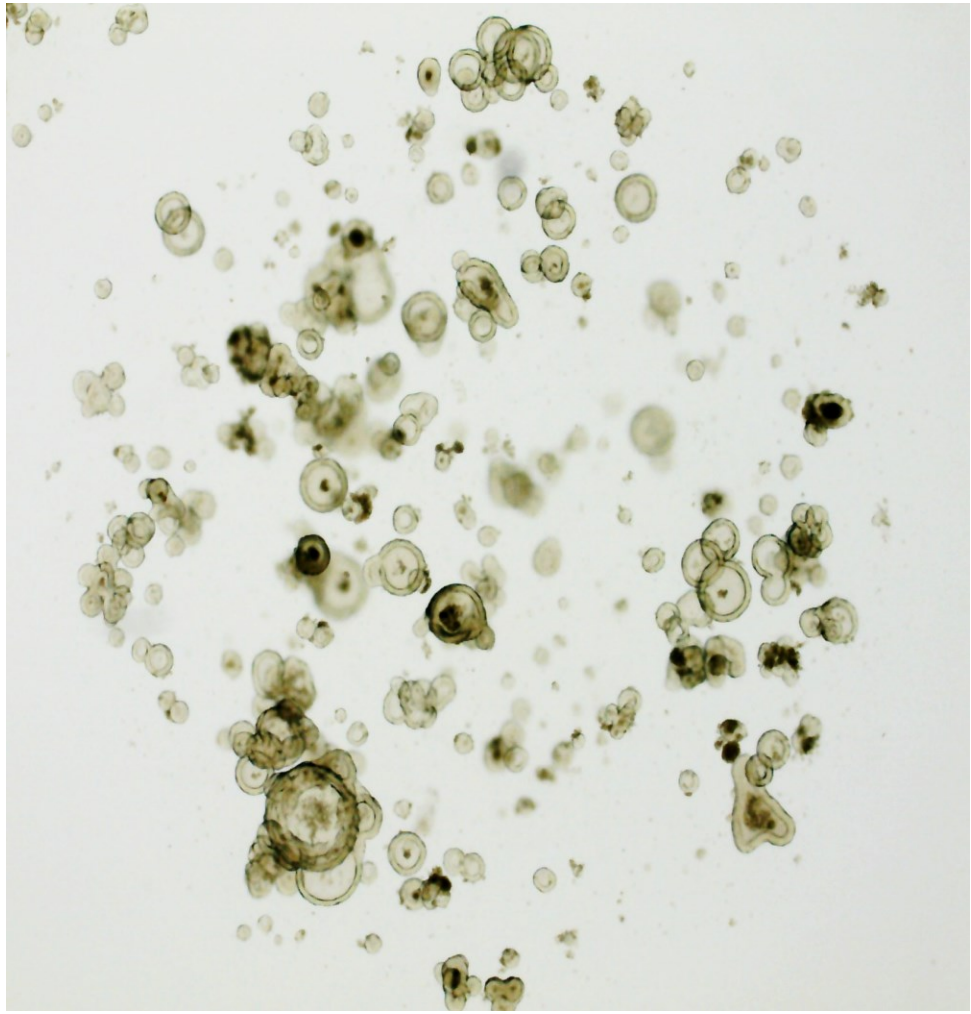
Materials and methods



Malene Spiegelhauer
Postdoctoral researcher

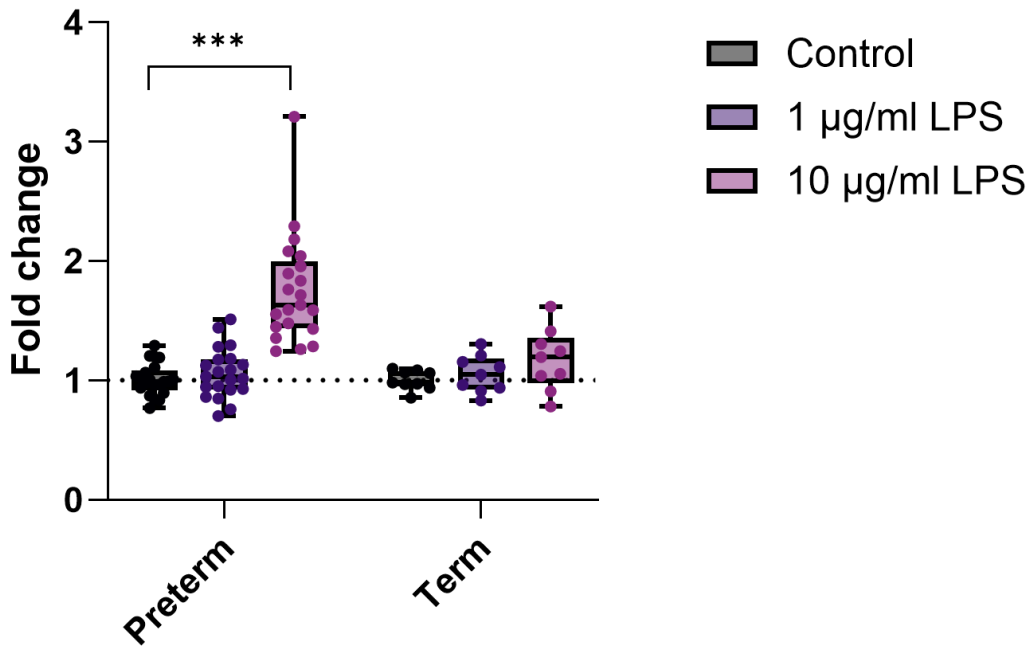
Preterm piglet intestinal organoids under the microscope



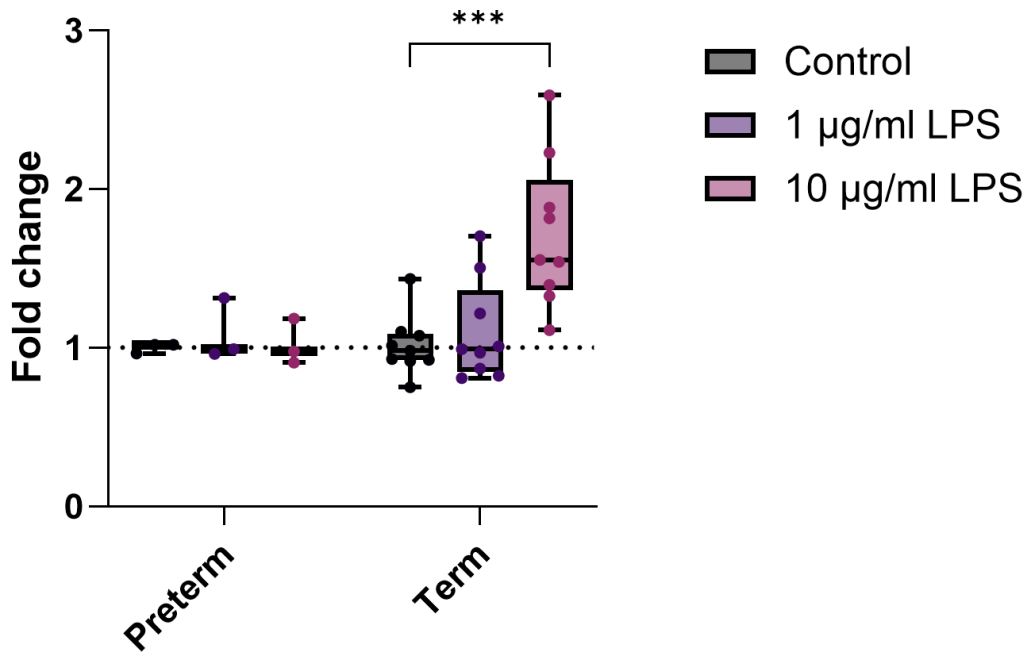


Interleukin-8 response to lipopolysaccharide (LPS) challenge

3D small intestinal organoids



3D colonic organoids



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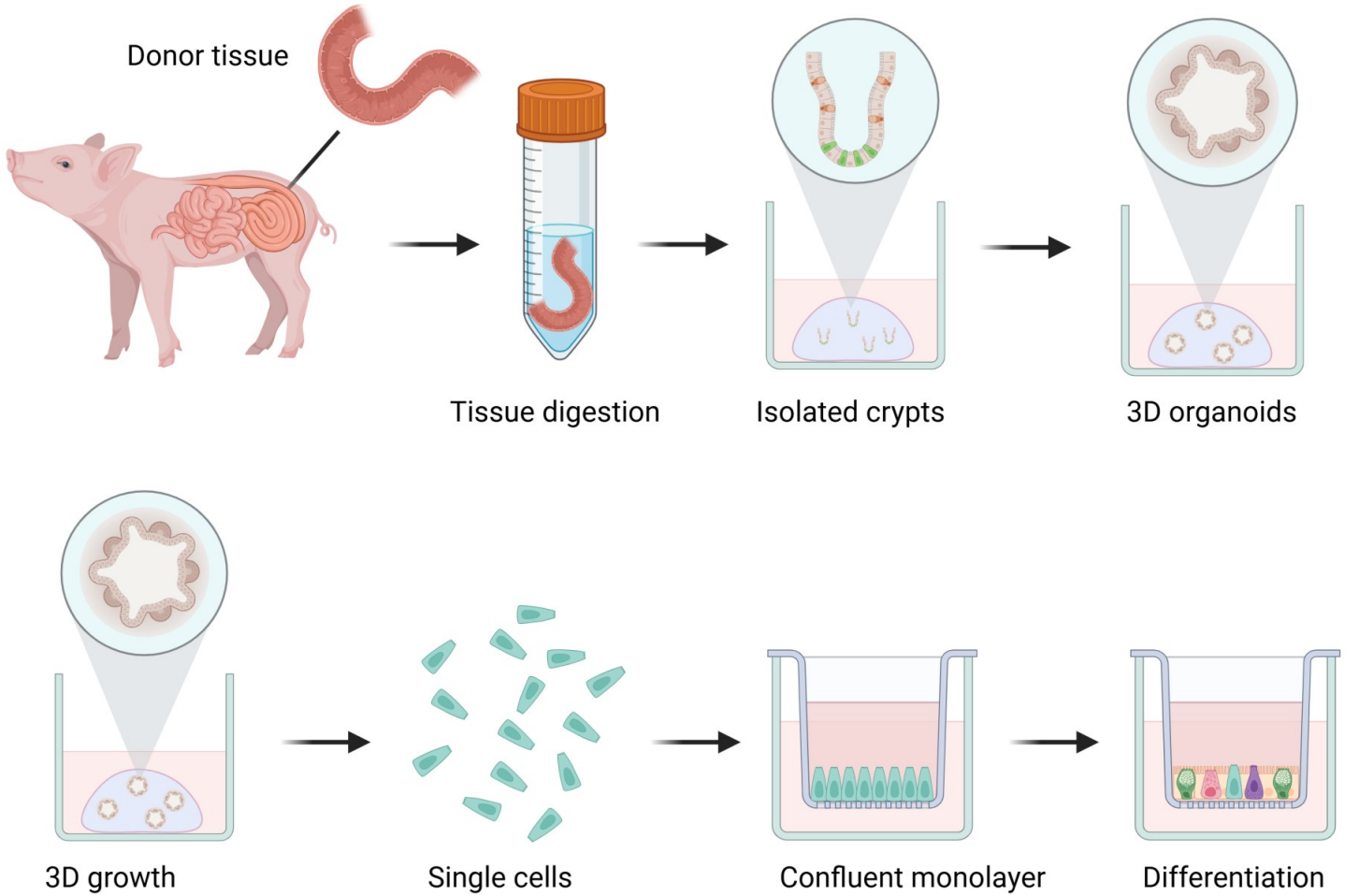

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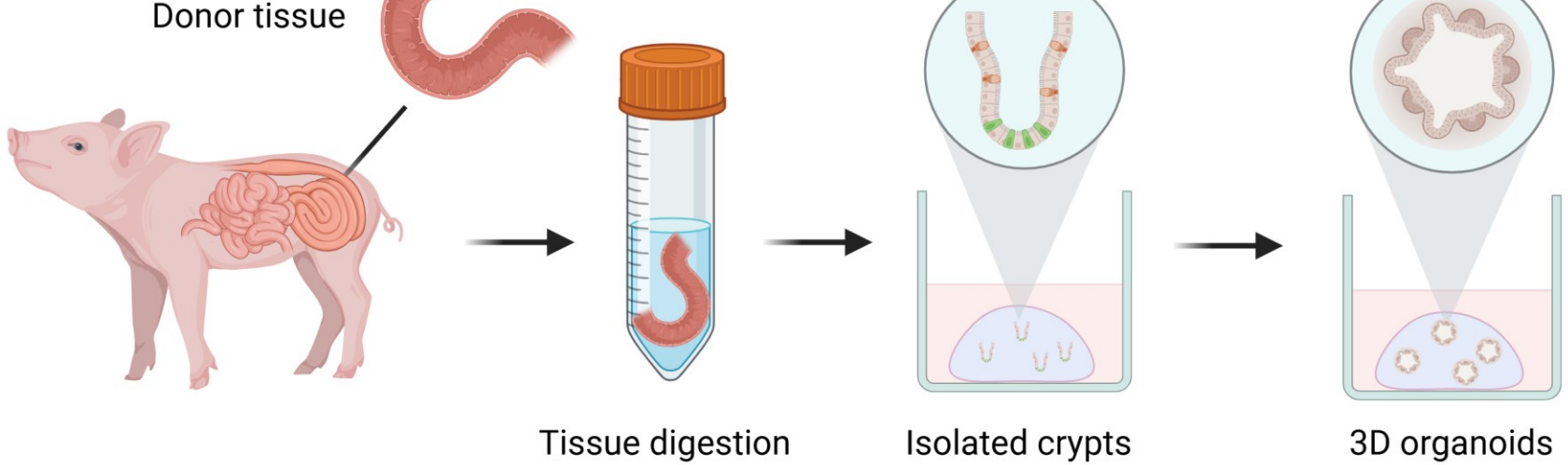

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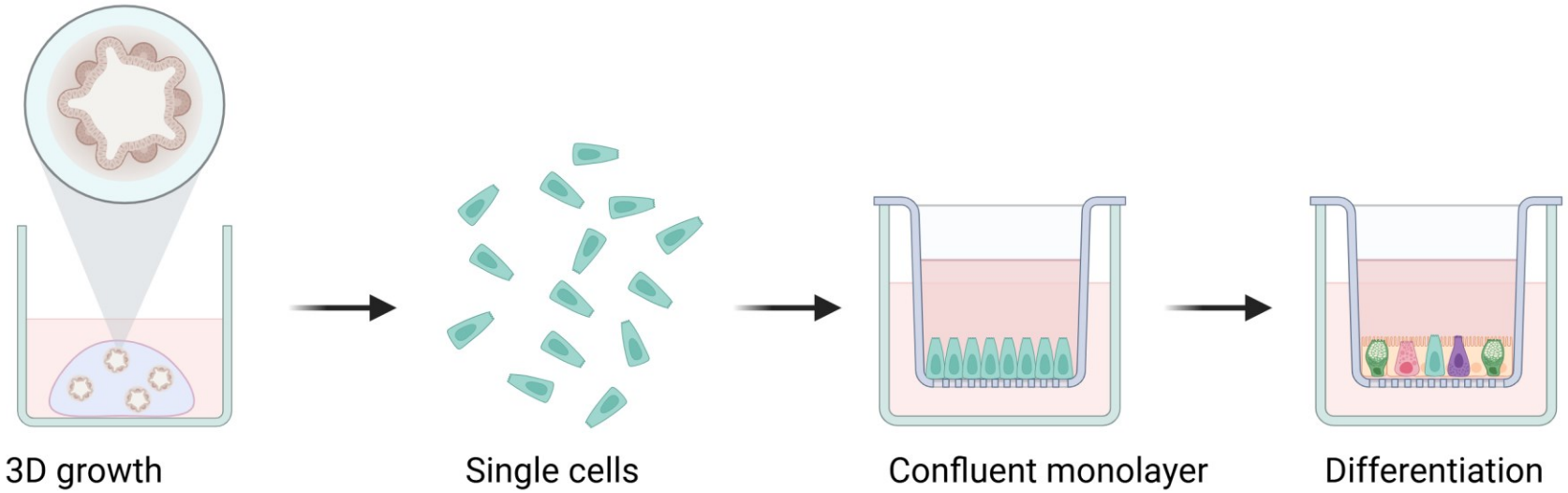

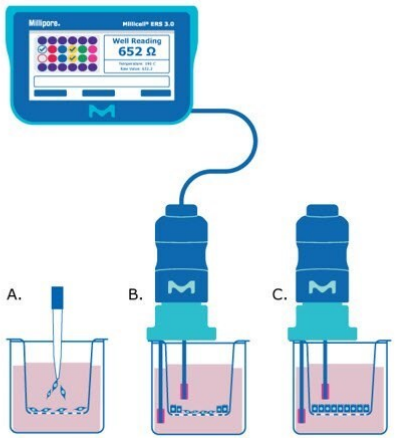

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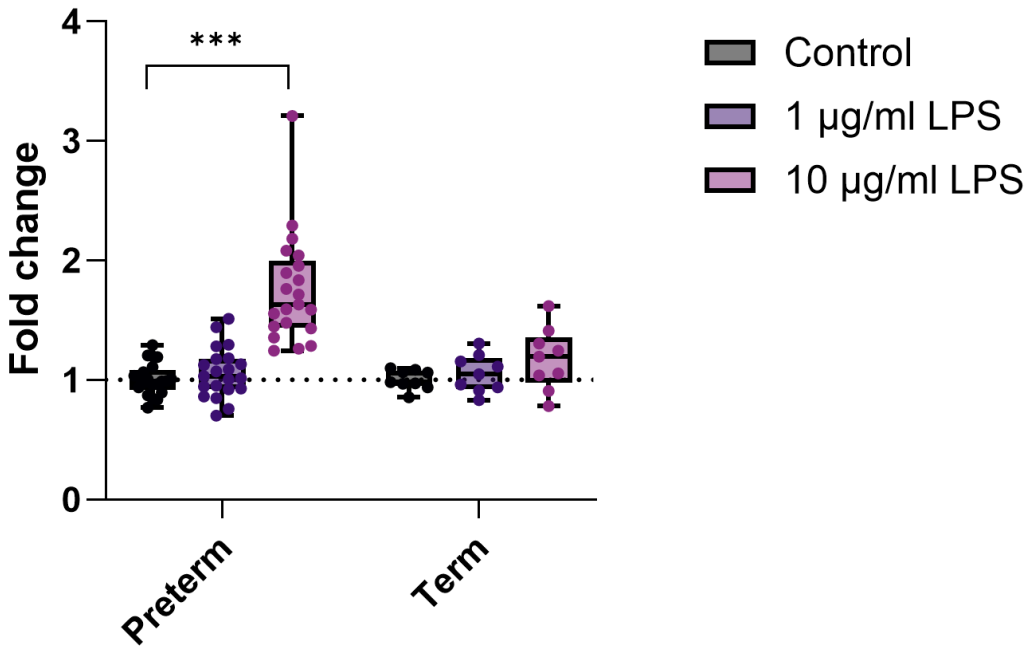
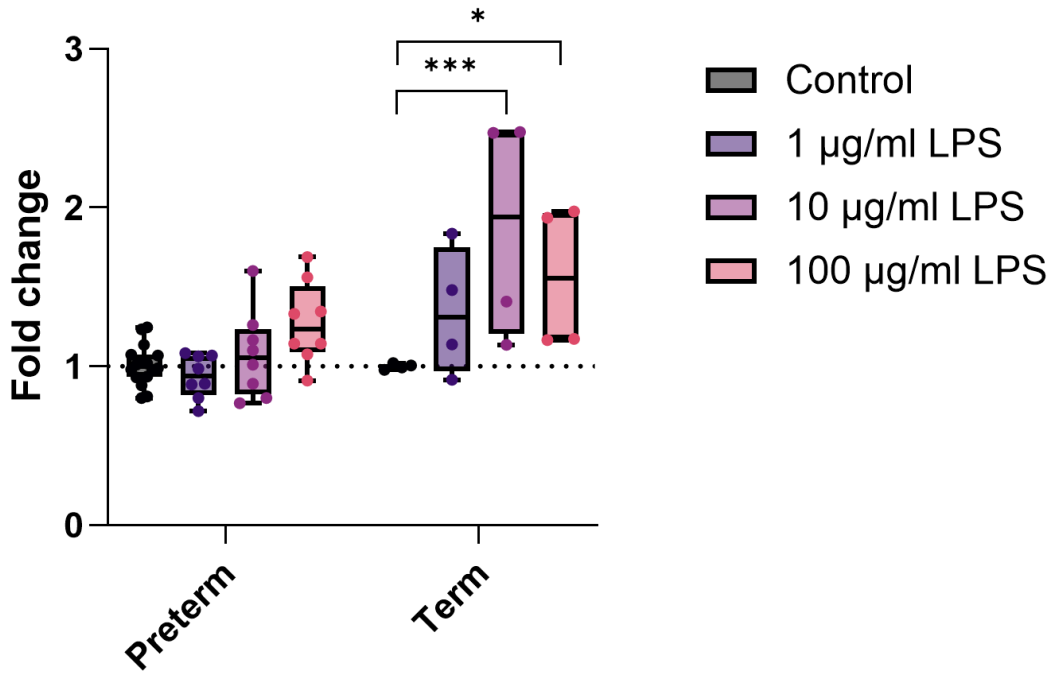


2D small intestinal organoids



Achievements and future perspectives

- Intestinal stem cells from preterm piglets are easily cultivable
- Spheric organoids can be transformed into monolayers that create and maintain barrier property (e.g. electrical resistance, permeability marker)
- Immune response to LPS depends on gestational age, gut segment and differentiation state

Ideally this in vitro model could replace live animals specifically for

1. Drug screening purposes
2. Initial dose-findings
3. Mechanistic underpinnings (e.g. microbe-host interactions)