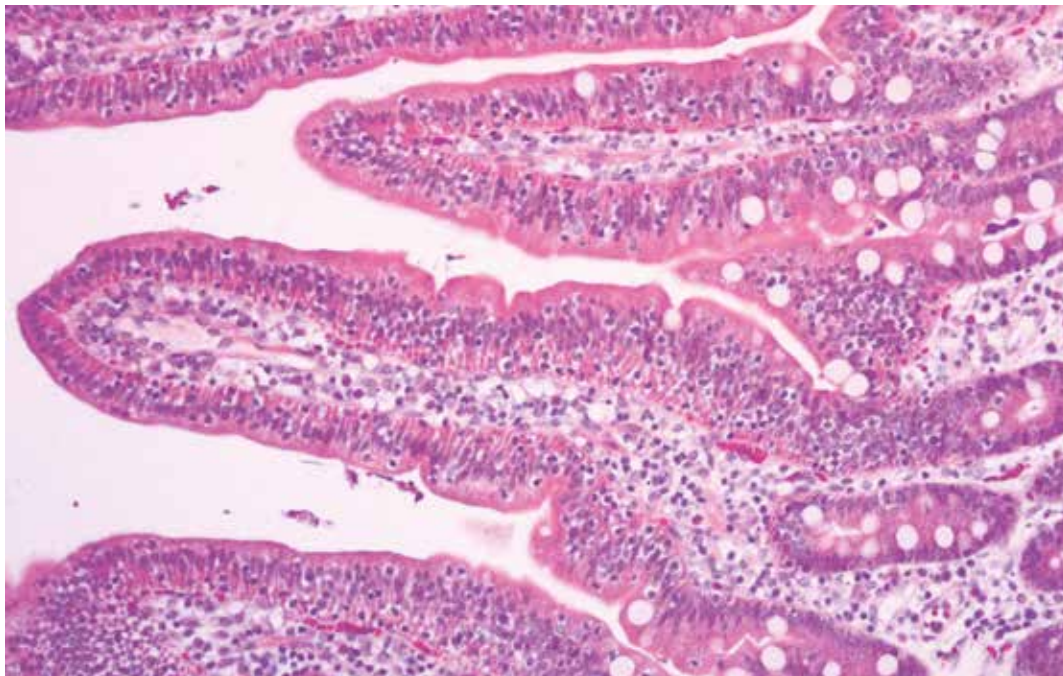


InTESTine™

PHYSIOLOGICALLY RELEVANT INTESTINAL TISSUE MODEL



TNO innovation
for life

TNO recently developed InTESTine™ in order to study the absorption and translocation of pharmaceutical, biological and nutritional compounds across the intestinal wall in a physiologically relevant model. This system uses fresh ex vivo intestinal tissue mounted into a two compartment model. So far, this has been the missing link in our toolbox to accurately predict absorption, oral bioavailability and PK of compounds.

The morphology and function of the intestinal tract changes from duodenum to colon with respect to thickness of the mucus layer, height of the villi, pore size of the tight junctions, expression levels of transporters, receptors and/or metabolising enzymes. With the InTESTine™ system different physiological processes can be studied using ex vivo intestinal tissue. The system is based upon published Ussing chamber techniques with some major advantages, including a higher throughput, a disposable multi-well setting, and standardized culture conditions in a humidified high-oxygen/CO₂ incubator on a rocker platform.

An unique feature of InTESTine™ is the opportunity to study multiple segments (duodenum, jejunum, ileum & colon) in parallel, under controlled conditions. Due to the presence of the mucuslayer, intestinal processes can be studied following exposure to digested samples, and in the absence or presence of microbiota. This clearly demonstrates the additional value of InTESTine™ compared to Caco-2 cells in order to study absorption, metabolism, food-drug interactions, and/or food-microbiota interactions of orally administered compounds.

TNO InTESTine™ SYSTEM

Freshly isolated healthy intestinal tissue from pigs is used in the InTESTine system. The gastrointestinal tract of pigs, like humans omnivorous, shows great similarities with the human GI tract. The main advantage of using pig tissue is the high availability along the whole GI tract. By removing the outer muscle layers, we can study the absorption, metabolism and complex integrated physiology occurring in the intestinal tissue in a cost-effective way.

An overview of the features of the Ussing chamber and TNO's InTESTine™ system is presented below.

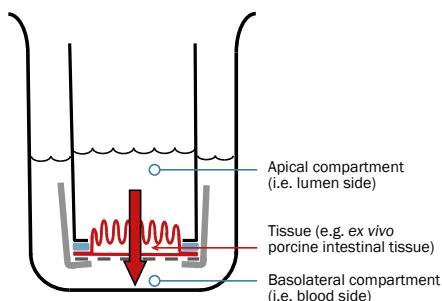


FEATURES

Unique to the InTESTine™ system is the opportunity to study transport, translocation, and/or interaction of compounds:

- › Across multiple and various segments (duodenum, jejunum, ileum, colon) in parallel. This will allow you to determine the 'window of absorption' in order to adapt the formulation of your compound
- › After several time points
- › In the absence or presence of intestinal permeability disturbance (e.g. mucolytic agents, microbiota, cytokines)
- › In the absence or presence of various (digested) food compounds

Porcine intestinal tissue in InTESTine



COMBINED SERVICES

InTESTine™ services can be easily combined with other platforms and techniques, including:

- › TNO's dynamic gastrointestinal model (TIM) (e.g. exposure to digested samples, in the absence or presence of microbiota)
- › Studying the release of satiety hormones (e.g. GLP-1, GLP-2, PYY, CCK)
- › Studying early immunological responses
- › Gene-activity analyses (transcriptomics)
- › Modeling services



	Ussing chamber assay	TNO InTESTine™
Throughput	Low	Medium
Chambers /system	6-12	24-96
Exposure area	0.005 - 1.27 cm ²	0.2 - 0.8 cm ²
Chamber Volumes	0.8 - 5 mL	0.5 - 7.5 mL (variable)
Environment	Permanent on lab table, chambers carbogenated by gas bubbling, 37°C water jacket	Complete system in incubator high oxygen, 5% CO ₂ , 37°C, humidified
Movement	Low, system is static, liquid circulation by gas bubbling in each individual chamber	High, system is placed on a shaking/rocker platform
Evaporation	High, can be prevented by rubber stoppers	Low, due to humidified incubator and no gas bubbling
Start	Chambers mounted one after each other	Chambers mounted simultaneously
Orientation of tissue	Vertical	Horizontal
Study with digested samples, microbiota, nanoparticles	No direct contact with tissue due to vertical mounting	Direct contact with tissue due to horizontal mounting

TNO.NL

TNO HEALTHY LIVING

TNO initiates technological and societal innovation for healthy living and a dynamic society.

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