

## Non Clinical Models



### Therapeutic areas

#### DERMATOLOGY

##### On Reconstituted 3D Human Epidermis

**SAFETY:** SKIN BIOCOMPATIBILITY and TOLERANCE BY MULTIPLE ENDPOINT ANALYSIS (MEA) and ACCORDING TO ISO 10993-23

- Oxidative stress
- Retinoids mechanism of action
- Stratum corneum peeling
- Stratum corneum lamellar structure restoring
- Epidermal renewal
- Skin Dryness: moisturizing efficacy
- Re-epithelization
- Skin atrophy
- Biorestructuring
- Inflammasome
- Ommuno-Competent Models (3D Tissues in co-culture with THP1 Monocytes)
- Epidermal barrier impairment
- Epidermal barrier protection and long-lasting effect
- Film Forming
- Protection against Exposome (UVs, pollen, blue light, pollution)
- Hyperosmolarity and hyposmolarity
- Hypoxic stress
- Chilling: cold stress
- Atopic Dermatitis: RHE colonized with *S. aureus*
- Immuno-competent Atopic Dermatitis Model: 3D Tissues In Co-Culture with THP-1 monocytes
- Psoriasis
- UV mediated immuno-suppression
- UV Induced Damages
- Senescence
- Photo-irritation and protection from photo-irritation
- Protection against systemic induced photo-toxicity
- Protection against pathogens: bacterial and yeast adhesion (strains to be selected)
- Biofilm prevention/reduction/eradication
- Skin microbiome: competition with established resident flora, prebiotic, probiotic, postbiotic activity, microbiome safe
- Skin penetration and diffusion on intact and injured epidermal models

##### On Full Thickness Skin

- Glycation
- UV A induced Photo-aging: dynamic model 10 days
- Wound healing and skin regeneration (scars)
- Anti-aging
- Acne-lesions with/without *C. acnes*
- Inflammaging
- Re-pulping: ECM boosting
- Skin firmness: counteracting atrophy
- Aged skin biorevitalization
- Striae distaense model
- Strengthens the dermo-epidermal junction
- Strengthens the extracellular matrix

- Filler model applicable to injectables
- Biofilm formation on infected wounds
- Diabetic ulcers
- Implants compatibility

### Photo-Dermatology on Reconstituted 3D Human Epidermis in Presence of Melanocytes

- UV activation and melanogenesis: pigmentation, depigmentation, Vit.D
- Skin pigmentation/depigmentation on sterile and colonized epidermal models
- Oxidative stress
- Tan activator
- Protection from UVA and UVB induced DNA damages
- Protection against melanocytes toxicity induced by yeasts
- Colonized models on pigmented RHE

### VitroScreenORA™ Dermis: Scaffold Free Spheroids

- Physiological senescence and senolytic efficacy
- UVA induced senescence
- ECM deposition and remodelling
- Targeting wrinkle's biomarkers
- Deep moisturization
- Modeling dermis disorders (fibrosis)
- Co-culture with adipocytes/melanocytes/ keratinocytes (customized protocols)
- Systemic exposure applicable to nutritional ingredients, secretomes and postbiotics
- Personalized dermis models: biological response of fibroblasts from different donor's age and ethnicity

### VitroScreenORA™ Vascularized Dermis

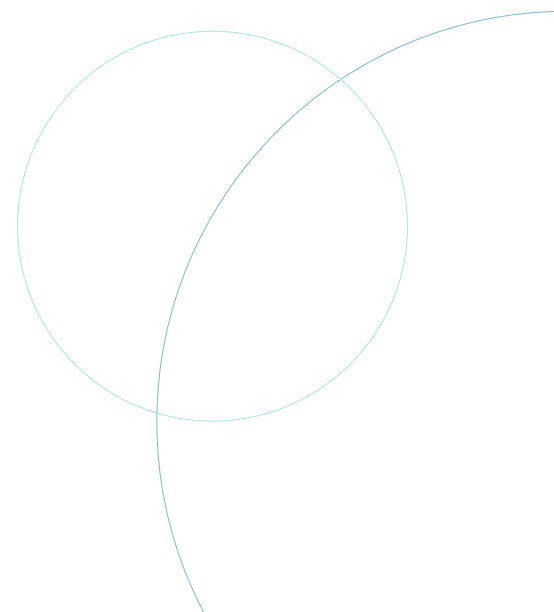
- Hypoxia effects on vasculature and angiogenesis
- Microvasculature structure modifications
- Photo-damage on vasculature
- Pro-inflammatory damages

### VitroScreenORA™ Dermal Papilla and Vascularized System

- Hair cycling anagen/catagen transition
- Catagen involution system
- Anagen metabolic phase to investigate hair growth on long-term treatment
- Anti-hair loss and hair growth efficacy
- Protective action against stress conditions (e.g. hyper-osmosis)
- Vascularized dermal Papilla: screening of actives for hair growth modulation

### VitroScreenORA™ Adipose Tissues

- Persistent organic pollutant (POP): toxicological screening
- Adipogenesis and lipolysis
- Lipid accumulation
- Lipid destock: slimming, plumping, resculpting
- Metabolic disorders simulation after long-term exposure (3 weeks)
- Influence of hormones
- Inflammation and Fibrosis
- Personalized models for metabolic profiling (age, sex)



## GASTROENTEROLOGY AND LIVER DISEASES

### On 3D Reconstituted Human Oesophagus Mucosa

- Biocompatibility (mucosal irritation according to ISO 10993-23)
- Film forming properties
- Muco-adhesion
- Re-epithelization
- Barrier properties restoring after chemical (low pH) induced damage: GERD model
- Tight Junctions boosting and protection
- Epithelial absorption and penetration

### On 3D Reconstituted Human Colon Epithelium

- Biocompatibility (mucosal irritation according to ISO 10993-23)
- Film forming properties
- Muco-adhesion
- Re-epithelization
- Osmotic mechanism of action
- Epithelial absorption and penetration study

### On 3D Human Intestinal Models

- Intestinal passage, transport and absorption
- Intestinal metabolism (customized)
- Inflammatory disease modeling (induced by cytokines mix)
- Monocyte epithelial adhesion assay (IF)
- Immuno-modulatory activity of prebiotics and probiotics
- Film forming and persistency properties
- Immunocompetent gut (co-culture with THP-1 cells model)
- Barrier function structure impairment and boosting
- Leaky gut syndrome based on Glutamine deprivation
- Bacterial adhesion, growth, survival, interaction and cross talk with intestinal cells
- Competitive adhesion to the intestinal mucosa
- Competition with bacterial 'secretome'
- E. coli invasion model
- Rotavirus like stress model

### On VitroScreenORA™ Intestine

- Intestinal and digestive health
- Metabolic competence applicable to pro-drugs ( under development)
- Immuno-mediated inflammatory Bowel Disease (IBD)
- Interaction with immuno-competent cells and microbiota secretomes
- Immuno-modulatory activity of prebiotics and probiotics
- Long-term experimental protocols with clinical relevance

### On Microliver Model

- Liver metabolism and cellular energy
- Hepatotoxicity : acute and chronic toxicity screening
- Metabolic competence: Cytochrome P450 activation/induction
- Liver steatosis
- Non-alcoholic Steatohepatitis (NASH)
- Hypercholesterolaemia

### On VitroScreenORA™ Adipe

- Application to Drug discovery and toxicological screening for personalized medicine
- Persistent organic pollutant (POP) toxicity studies
- Fatty acid oxidation (FAO) & mitochondrial dysfunction
- Adipogenesis and lipolyse
- Metabolic disorders simulation and long-term exposure
- Influence of hormones
- Inflammation and Fibrosis
- Personalized model for metabolic profiling
- Differential response to pro-inflammatory stimuli according to donor's phenotype

### On 3D Reconstituted Human Colon Epithelium

- Biocompatibility (mucosal irritation according to ISO 10993-23)
- Film forming properties
- Muco-adhesion
- Re-epithelization
- Osmotic mechanism of action
- Epithelial absorption and penetration study

## GYNAECOLOGY

### On 3D Reconstituted Human Vaginal Mucosa

- Mucosae toxicity and tolerance with multiple endpoint analysis (MEA)
- Biocompatibility (mucosal irritation according to ISO 10993-23)
- Film forming and Muco-adhesion: barrier protection
- Dryness model and Moisturization
- Re-epithelisation
- Decongestant and soothing efficacy
- Protection against bacterial adhesion/invasion (strains to be selected)
- Anti-bacterial activity
- Protection against uropathogens (E. coli) invasion
- Anti-mycotic efficacy
- Probiotic protective efficacy
- Competition model with established resident flora/pathogens (co-colonization with *Candida Albicans* and *Lactobacilli* sp)
- *Lactobacilli* sp adhesion
- Innate immunity response
- Epithelial absorption and penetration study
- Assessment of MoA of ingredient and formulations: systemic and topical exposures

### On VitroScreenORA™ Endometrium

- To monitor the evolution of a dynamic organ-like model (donor's cells customized model)
- To recapitulate different phases of the menstrual cycle (proliferative or secretive)
- To monitor response to hormone exposure during 3 weeks

## OPHTHALMOLOGY

### On Human Corneal Epithelium, HCE

- Acute eye irritation potential (OECD 492, OECD 492B)
- Biocompatibility after acute exposure: highly discriminating model for mild irritants
- Evaluation of acute and cumulative(3 days) ocular toxicity for preservatives and other critical ingredients screening
- Discomfort and recovery after acute and repeated applications
- Corneal binding and film forming properties
- Osmotic stress (hyper-osmolarity and hypo-osmolarity)
- Experimental Dry Eye in vitro (EDEV-3 levels damages)
- Ocular surface inflammation
- Corneal re-epithelization and 'debridement' model
- Protection against bacterial adhesion (strains to be selected)
- Immuno-competent HCE
- Immuno-competent EDEV (co-culture model)
- Corneal epithelium absorption , penetration and metabolism
- Protection against Exposome (UVs, pollen, blue light, pollution)
- Oxidative Stress Induced Damage
- Film forming activity

### On VitroScreenORA™ Corneal Stroma

- ECM formation, assembly and remodeling
- Simulation of chronic fibrotic disease
- Keratoconus model
- Photo-damage keratitis UVA/UVB-induced
- Screening of active compounds

## ORAL CARE

### On 3D Reconstituted Human Oral or Gingival Mucosa

- Biocompatibility (irritation potential) according to ISO 10993-23
- Film forming and persistency properties
- Protective efficacy on barrier function and long lasting effects
- Re-epithelisation and regenerating efficacy
- Decongestant efficacy
- Anti-inflammatory efficacy
- Aphthous lesions
- Competition with established resident flora/pathogens
- Protection against bacterial adhesion (strains to be selected)
- Anti-fermentative activity
- Antiplaque and anti-cavity efficacy (S. mutans model)
- Epithelial absorption and penetration study

## RESPIRATORY

### On 3D Reconstituted Human Nasal, Bronchial and Lung Epithelia

- Cilia Beating and mucociliary clearance (partnered)
- Film forming and barrier function strengthening properties after single and repeated exposures
- Inflammation
- Oxidative stress associated to PM exposure
- Re-epithelization and nasal wound healing
- Decongestant efficacy
- Phagocytosis assay: protection against pollens and pollutants
- Ferning Assay: Mucolytic Efficacy
- Cilia ultrastructure (SEM analysis)
- Protection against exposome (particulate matter, sensitizers, pollens, pathogens, viruses: adhesion and defence mechanisms)
- Protection against bacterial adhesion (strains to be selected)
- Competition with established resident flora/pathogens
- Efficacy in disrupting established biofilm
- Efficacy in preventing biofilm formation
- Trans-epithelial passage
- Inhalatory toxicity (liquid or nebulized)
- Biocompatibility (mucosal irritation) according to ISO 10993-23
- Immuno mediated response: co-culture models with THP-1 cells
- Probiotics adhesion and growth
- Innate immunity boosting ( co culture with THP-1 cells)
- Epithelial absorption and penetration study

## UROLOGY

### On 3D Reconstituted Human Bladder Mucosa

- Film forming activity and persistency
- Protection of barrier integrity
- Inflammation
- Anti-bacterial adhesion
- Anti-biofilm activity
- Protection against bacterial damage
- Epithelial absorption and penetration study
- Assessment of MoA of ingredient and formulations: systemic and topical exposures

### On VitroScreenORA™ Prostate

- Metabolism applied to prodrugs
- PSA production
- 5- $\alpha$ -reductase model: TST conversion in DHA
- Dihydrotestosterone release



## Microbiome Research Unit

### MICROBIOLOGICAL SCREENING

- Definition of MBC
- Definition of MIC
- Biofilm by crystal violet plate method
- Interference on bacterial growth and metabolism
- In vitro sniff test
- Customized Microdilution Assays

### COLONIZED 3D HUMAN RECONSTRUCTED TISSUES

- Bacterial Adhesion: boosting or inhibiting bacterial growth and proliferative capacity
- Anti-bacterial Efficacy
- Anti-mycotic Efficacy: skin and nails
- Bacterial and Yeasts competition models: skin, scalp, mucosae
- Microbiome impact on barrier function: development, innate immunity, specific pathways modification
- X-biotics MoA and Efficacy: pathogens inhibition and recognition
- Wound healing on infected tissues
- Microbiome safe claim
- Anti-Fermentative, Anti-Cavity and Anti-Biofilm Formation on Gingival Mucosa
- Healthy site specific microbiome model

### DISEASE MODEL

- Atopic Dermatitis: *S. aureus*
- Acne lesions: *C. acnes*
- Scalp microbiota: Dandruff Model
- Biofilm models: anti-biofilm formation efficacy, influencing of EPS matrix production, biofilm disruption after acute or repeated treatments
- Microbiome role in aging and pigmentation
- Customized infected tissue models
- Infected wounds healing



## Medical Devices

### PHYSICAL, MECHANICAL AND CHEMICAL MEANS

- Customized Protocols: Ancillary Action Models to Exclude Ph.I.M. Mechanisms
- Film Forming and Persistency on Skin and Epithelia
- Boosting and Protecting Epithelial Barriers
- Muco-Adhesion
- Protection from Pollutants, Pollen, Allergens
- pH Modification
- Protection from Acid Damage
- Anti-Bacterial Adhesion
- Protection Against Bacteria Induced Damages
- Anti-Biofilm Properties and Efficacy in Biofilm Disruption
- Protection from Ultraviolet A and B, IR and Blue Light
- Cilia Beating, Phagocytosis and Mucociliary Clearance (Partnered)
- Soothing and Decongestant efficacy from Osmotic Stress
- Moisturizing Efficacy: Skin, Mucosae
- Re-Epithelization, Wound Healing, Aphthe Lesions
- Antimycotic Efficacy on Skin and Nails