EVALUATION OF NANOPARTICLE INTERACTIONS WITH SKIN

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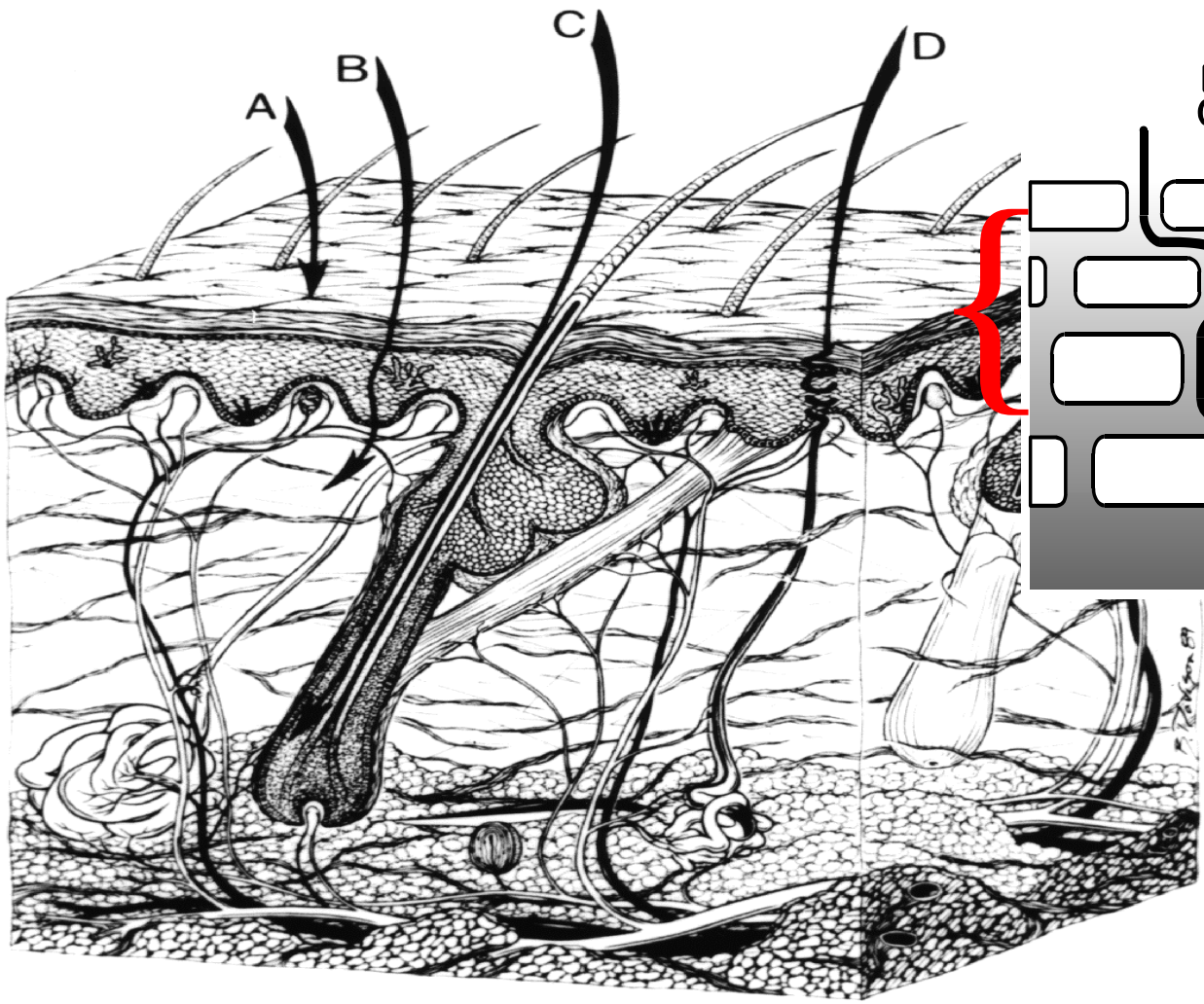
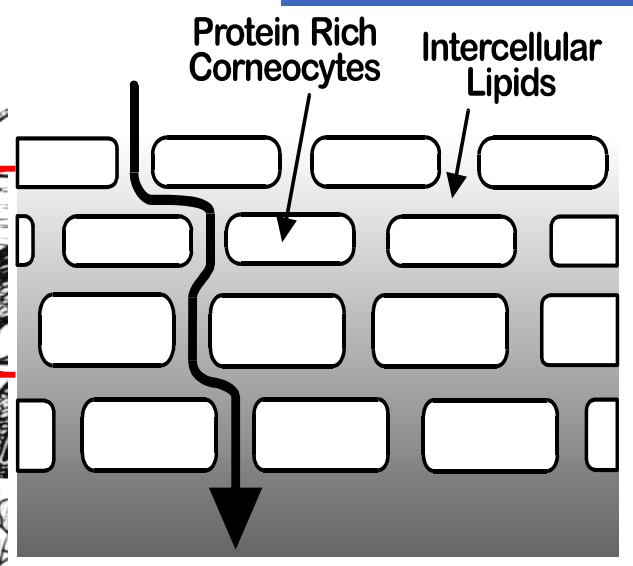
Overview

Focus of the proposed research is to assess the nature of interactions between manufactured nanoparticles and the skin.

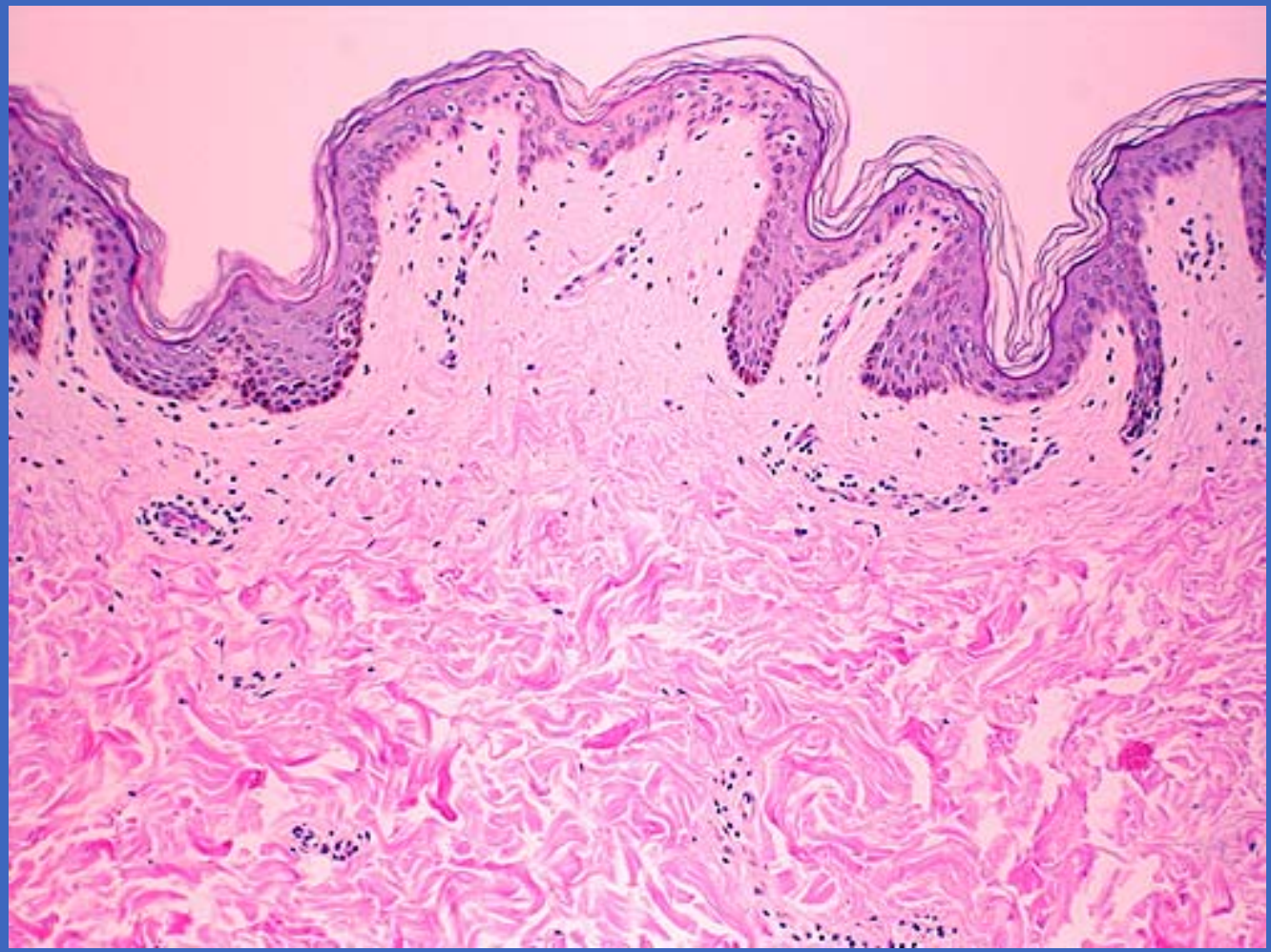
- Dermal absorption
- Cutaneous toxicity
- Distribution to skin after systemic exposure

Skin: PORTAL of entry and TARGET for toxicity

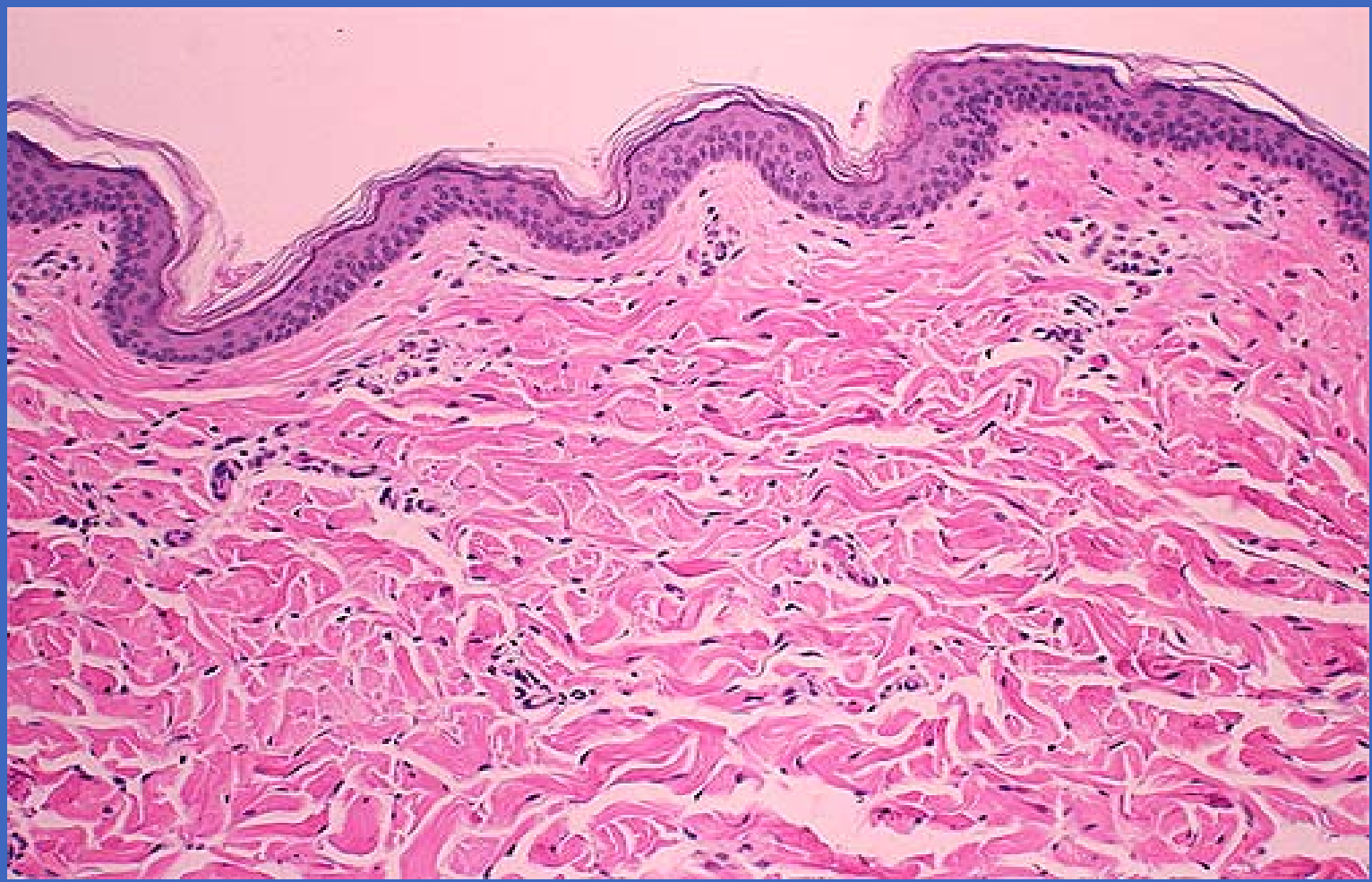




Human Skin



Porcine Skin



- Presently, there is minimal data available on the interaction of manufactured nanoparticles with the skin.
- Decontamination would be significantly different than with “traditional” chemical exposure since solubilization or dilution might be less efficacious.
- Basic requirement for a risk assessment includes information on hazard (e.g. toxicity) as well as exposure (e.g. absorption). This project should begin to define these boundaries.

Nanoparticles to be Studied

- Carbon Bucky balls and nanotubules
- Iron oxide nanocrystals
- Cadmium selenide nanocrystals

- Eight particles types selected to study effect of size, shape and composition

Model Systems

- Human epidermal keratinocyte cell culture
- Porcine skin flow through diffusion cells
- Isolated Perfused Porcine Skin Flap
  - Systemic uptake from perfusate
  - Assess absorption and toxicity of interesting particles

Experimental Design

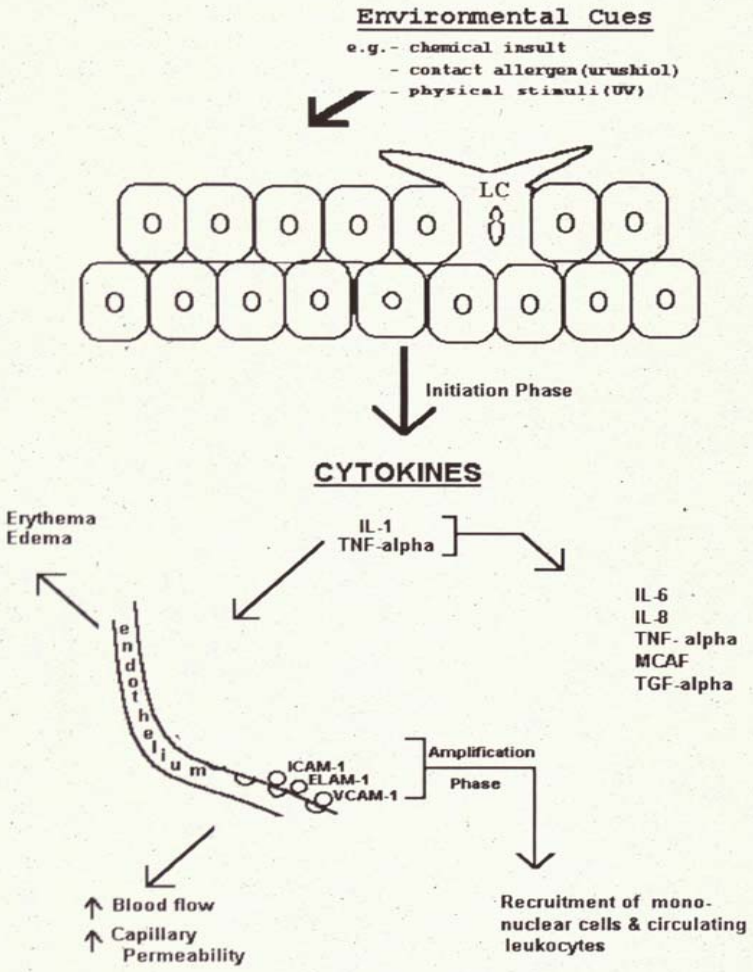
- Nanoparticles will be applied topically in three exposure scenarios
  - Neat
  - Water
  - Mineral oil
- Two Doses

Endpoints

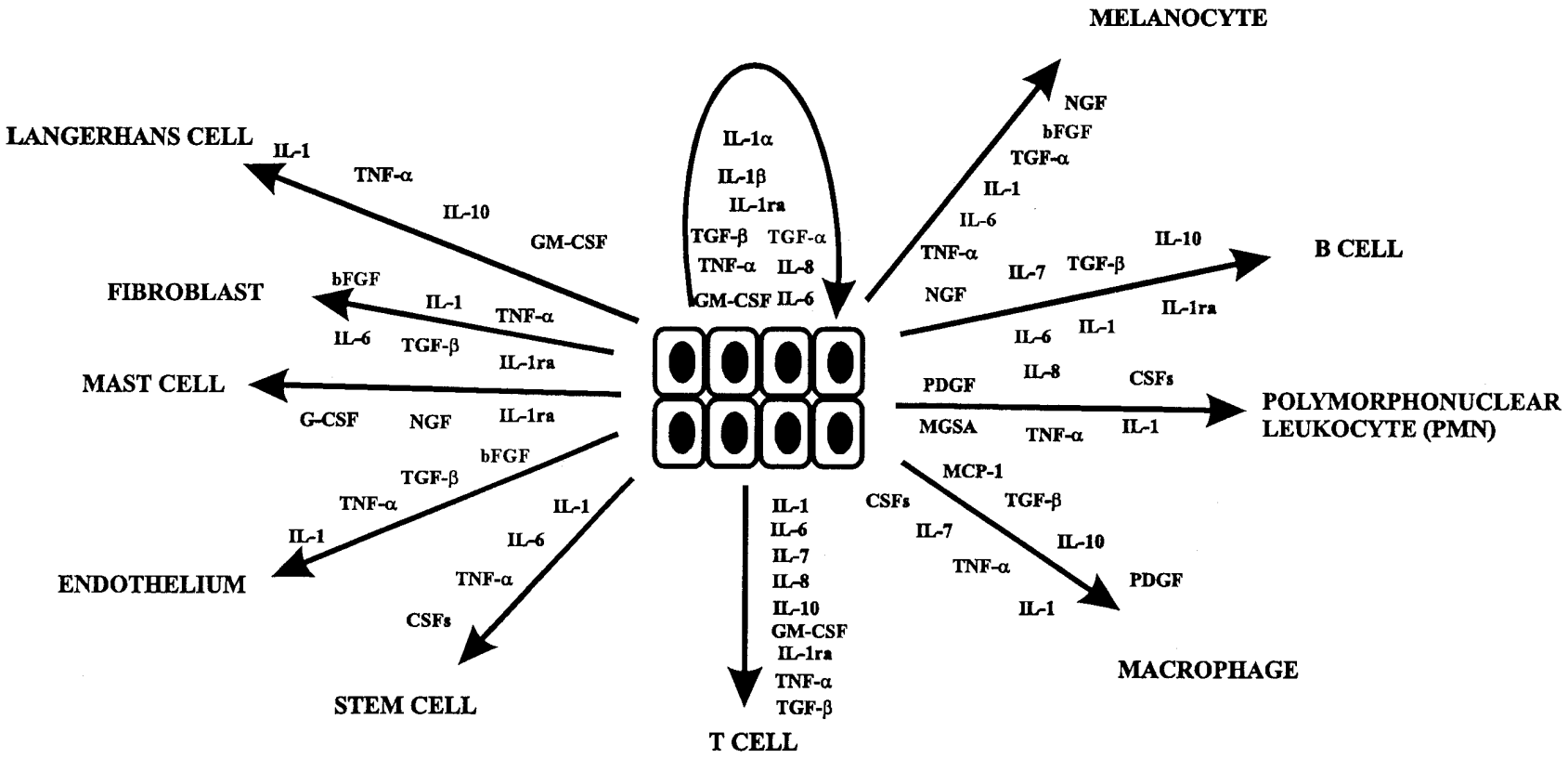
- Light and Electron Microscopy
- Cytotoxicity and IL-8 release

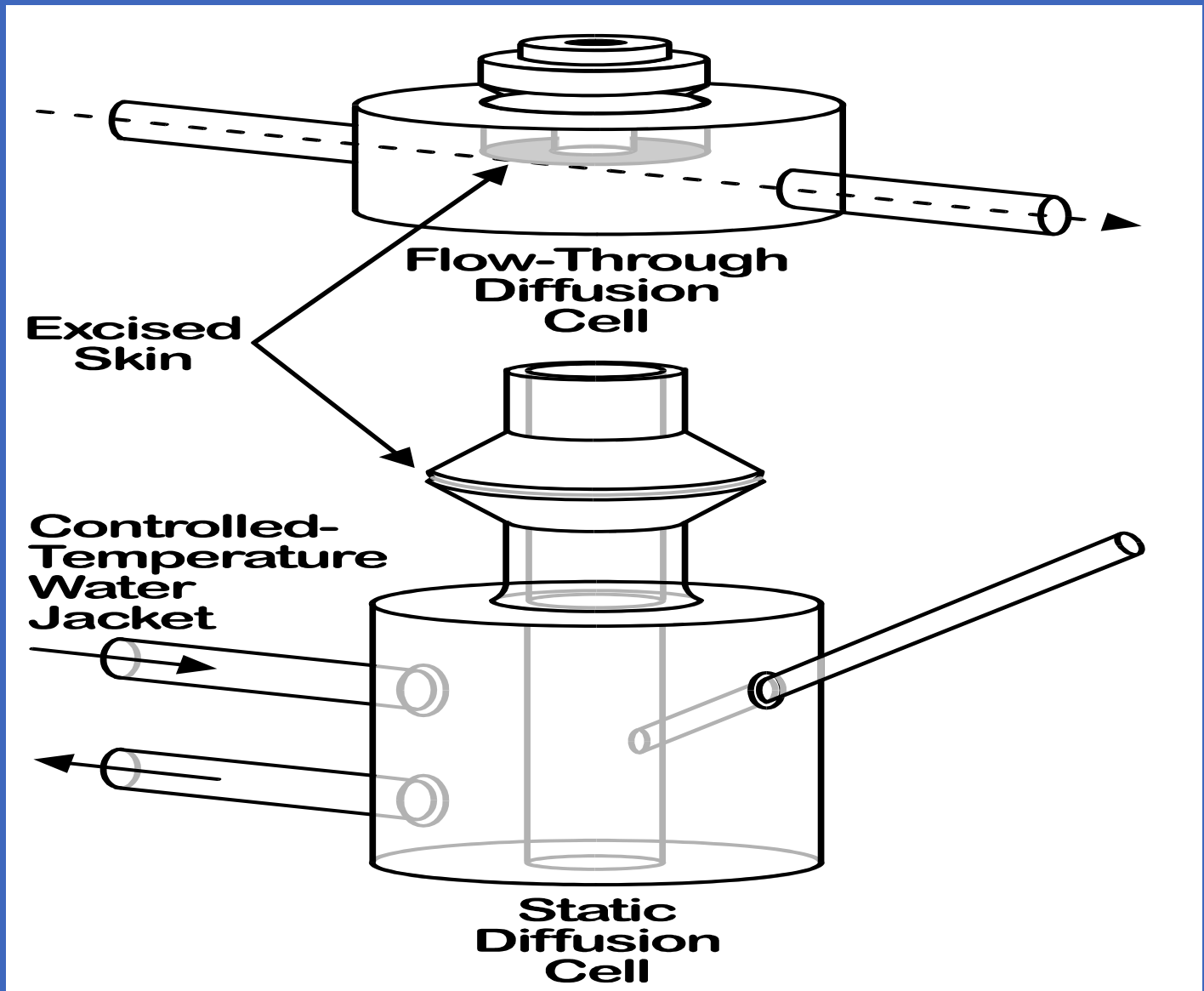
- Particles that demonstrate potential toxicity or absorption in simpler models will then be studied in the IPPSF

KERATINOCYTES CAN FUNCTION AS ENVIRONMENTAL SIGNAL TRANSDUCERS CONVERTING EXOGENOUS STIMULI INTO PRODUCTION OF PRO-INFLAMMATORY CYTOKINES



KERATINOCYTE CYTOKINE NETWORK

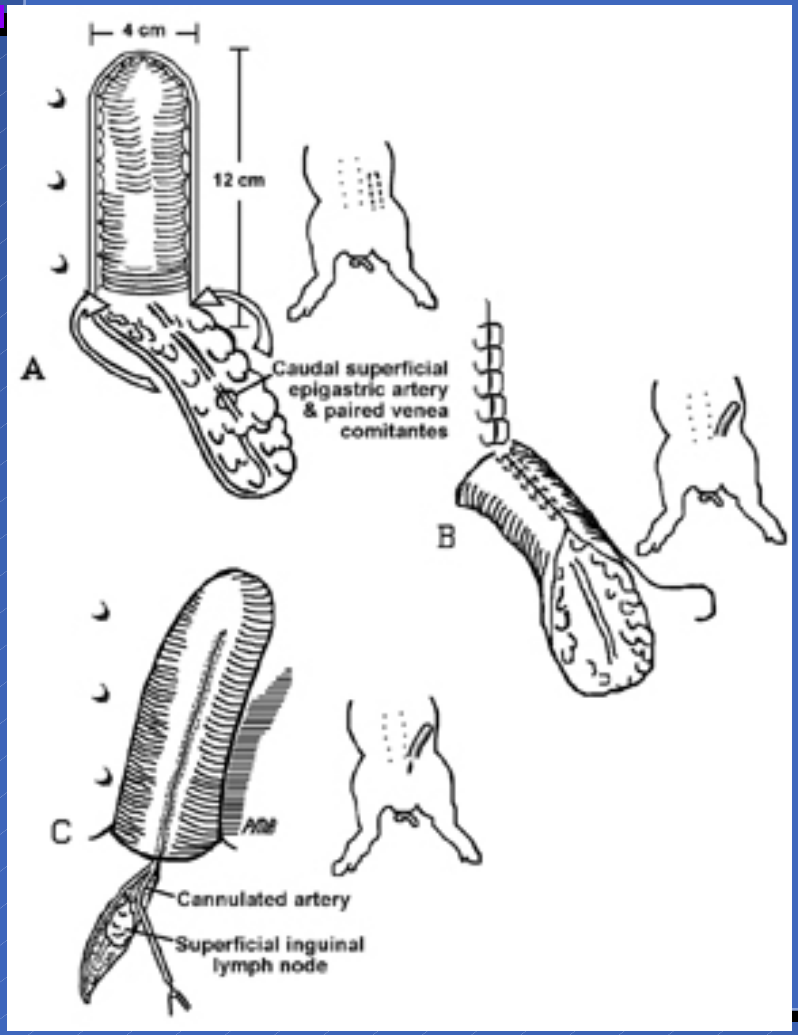


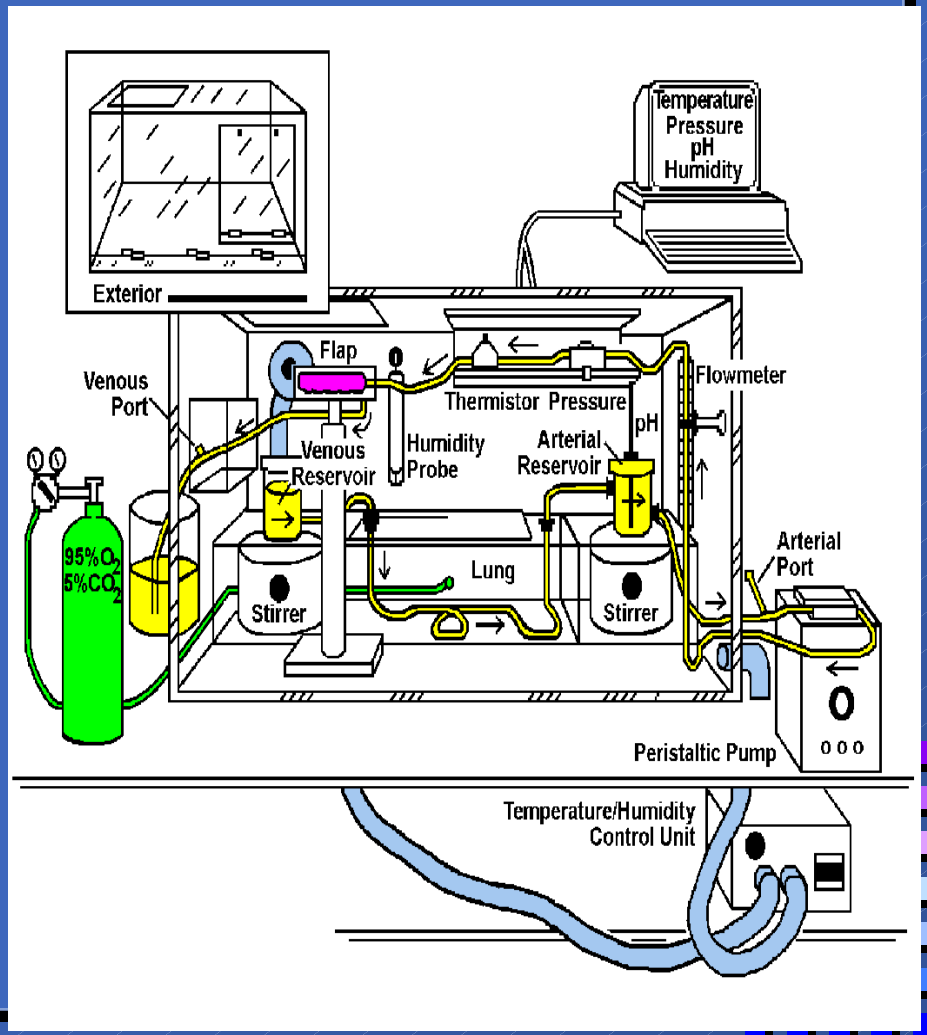

Flow-Through
Diffusion
Cell
Excised
Skin
Controlled-
Temperature
Water
Jacket
Static
Diffusion
Cell

Isolated Perfused Porcine Skin Flap (IPPSF)

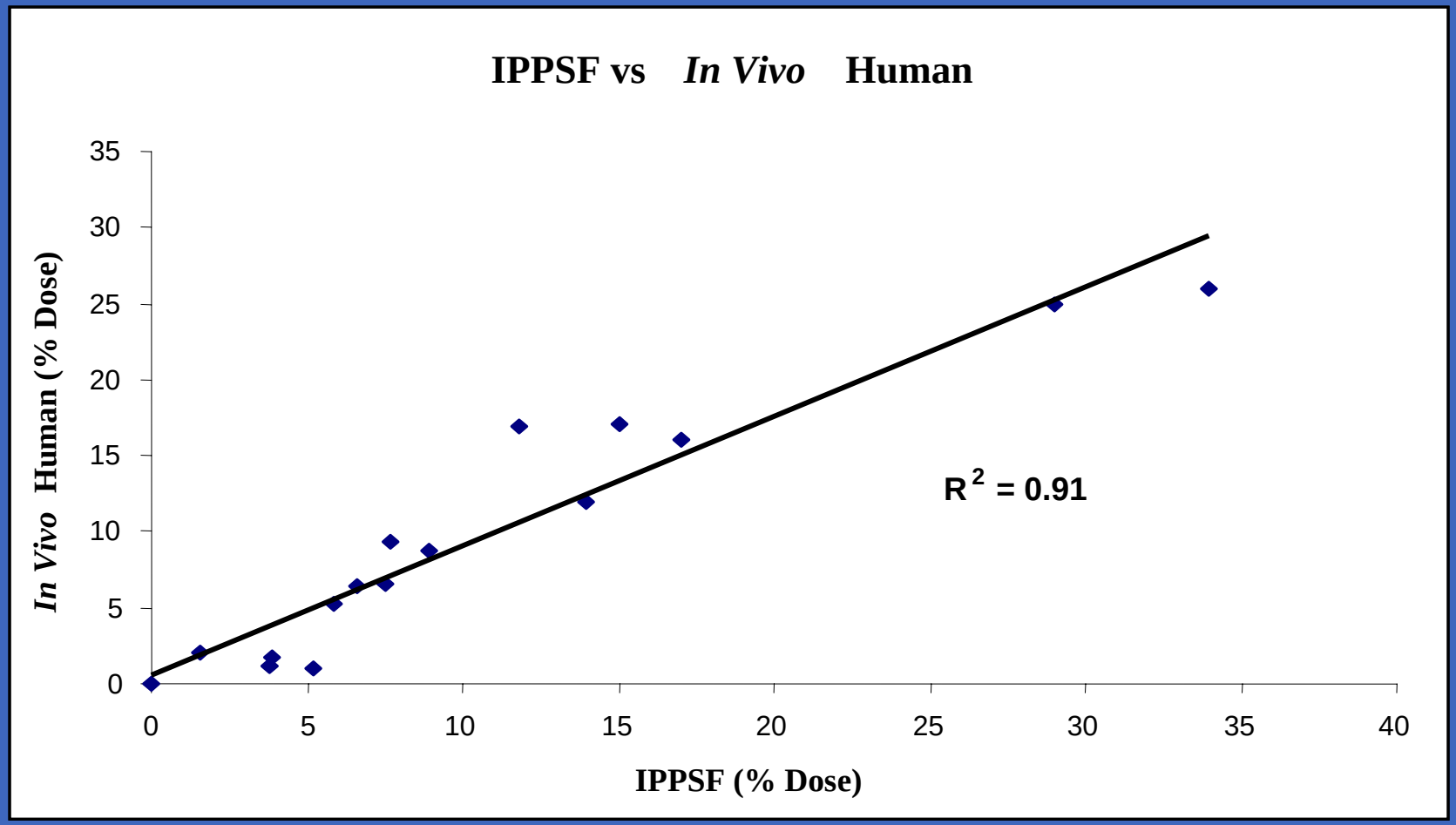
- Isolated system with control over physiological parameters and perfusate composition
- Intact functional microcirculation
- Viable epidermis and dermis
- Relatively large dosing area
- Predictable extrapolation to *in vivo*
- Allows for simultaneous assessment of absorption, skin disposition, pharmacokinetics and biomarkers of irritation
- Humane alternative animal model
- Cost-effective compared to *in vivo* studies

IPPSF Surgery and Perfusion Systems





IPPSF Closely Parallels *In Vivo* Human Absorption



Conclusion

- Work should provide data on ability of a range of manufactured nanoparticles to interact with skin
- Initial assessment of potential vehicle effects
- Should provide boundaries for a dermal risk assessment on manufactured nanoparticle exposure