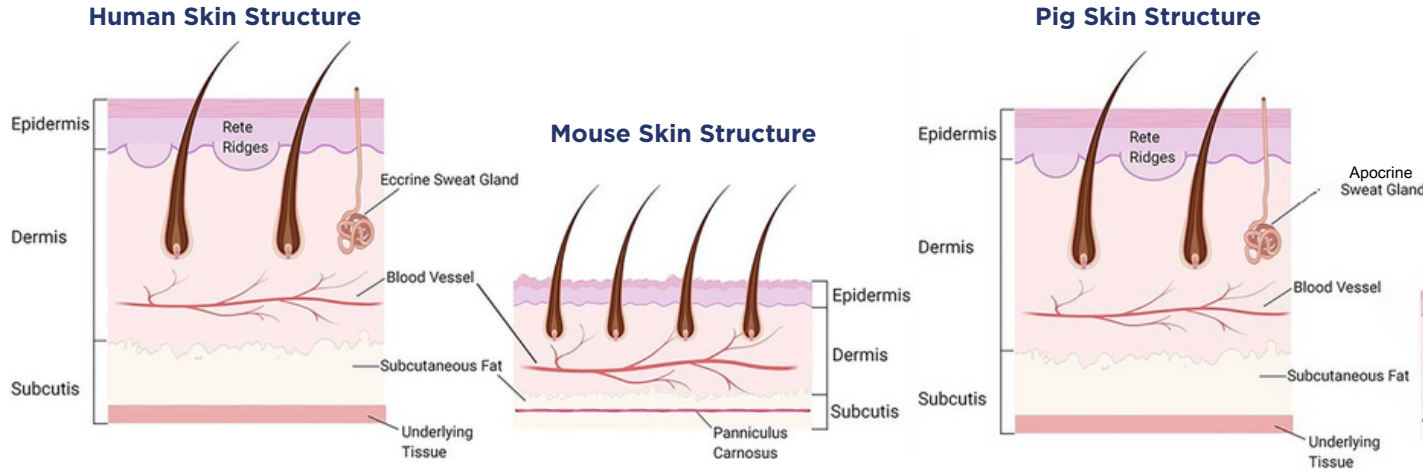
The Physiological Fidelity of Dermatological Research Platforms

The Problem

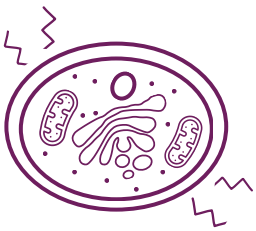
In dermatological research, selecting a **translatable animal model** with fidelity to human skin is paramount[1]. Rodent skin presents substantial limitations due to distinct anatomical and physiological properties compared to human skin. The thinner epidermis, different lipid composition, and higher hair follicle density significantly affects transdermal drug delivery and absorption, leading to **misleading interpretations** in pharmacokinetic and pharmacodynamic profiles[2].

Furthermore, these models fail to accurately replicate human skin responses in toxicology studies, as differences in skin barrier function can alter the penetration and local effects of chemicals. In cosmetic testing, these variations can impact the assessment of **efficacy** and **safety** of topical formulations, as the product absorption and interaction with skin cells does not accurately reflect human skin responses[3].



FA schematic showing the structure of human skin in comparison to the structure of mouse skin[10]

While human skin models, such as punch biopsies or skin organoid cultures, provide a closer approximation to in vivo human skin responses, they also come with inherent limitations[4],[5],[6],[7]. One significant challenge is the difficulty in **oxygenating** the core of the tissue effectively.



In vitro skin models inherently **lack proper vascularisation**, which supply the necessary oxygen and nutrients to the skin. This limitation leads to a state of **hypoxia**, inducing abnormal cellular stress responses affecting their behaviour and potentially altering results, especially in studies focused on metabolism, cellular proliferation, or wound healing processes. Ultimately, this impacts the **reliability** of these models in predicting in vivo outcomes.

Conversely, the pig is a more **comparable** and **physiological** species due to its similar epidermal thickness, stratum corneum composition, and lipid profiles, providing a more relevant platform for dermatological research. This resemblance extends to the evaluation of agrichemicals and household products, where pigs more reliably predict human dermal exposure and toxicity[8].

Despite the compelling anatomical and physiological similarities between pig and human skin, there are significant reasons why it is not the industry standard. The pig is a highly sentient being, so there are significant **ethical challenges** to consider. The **costs** associated with maintaining pigs for research are also considerably higher compared to small animal models.

FDA

In addition to financial and ethical considerations, the time involved in obtaining **regulatory approvals** for the use of pigs can be substantial. These factors make research with pigs a more **complex** and **time-consuming** endeavour, limiting its widespread use as the standard model for dermatological research[9].

The Solution

Ex-vivo technology can enable the use of porcine tissues without the associated time and economic constraints. Pebble has developed the world's first **physiological skin** and **entire limb** platform that fully mimics in vivo conditions. The **LIVING-SKIN** and **LIVING-LIMB** systems maintain cellular integrity and function through a process that effectively restores blood flow and replicates the physiological conditions of living organisms.

Pebble's MULTI-ORGAN system, incorporating a limb (left), liver (middle) and kidney (right).

The technology circumvents the limitations of traditional ex-vivo approaches by **preserving** the **natural homeostasis** of the skin, enabling more **accurate** and **reliable** results.

This advance allows precise studies of drug absorption, toxicological responses, and the effects of cosmetics and other chemicals, in a model that is **highly comparable** to human tissue.

The **efficiency** and **cost-effectiveness** of Pebble's systems present a compelling alternative to current industry standards. Being both **ten times faster** and **cheaper** than comparable large animal in-vivo systems, they offer the potential to expedite research processes. As a result, these systems will become the **new benchmark** for dermatological research, balancing scientific integrity, speed, and cost without compromising on ethical standards.

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