## Assessment of Nb<sub>4</sub>C<sub>3</sub> MXene Single-Cell Skin Interactions and Irritation Evaluation Using a Non-Animal Model: A Safe Material for Cutaneous Applications

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## Abstract

Transition metal carbides, nitrides, and carbonitrides (MXenes) are emerging as promising candidates for a growing list of biomedical applications [1-5], including skin-related uses such as artificial skin, wound healing dressings, and skin sensors. However, there is limited data available regarding the potential skin toxicity of newly synthesized MXenes such as Nb<sub>4</sub>C<sub>3</sub>.

Here, we investigated the interactions of Nb<sub>4</sub>C<sub>3</sub> MXene with human skin cells, utilizing both immortalized HaCaT cells and primary normal human epidermal keratinocytes (NHEK). To this end, we applied LINKED, our recently proposed label-free single-cell detection strategy based on single-cell mass cytometry by time-of-flight (CyTOF) [1], enabling nanomaterial detection and simultaneous measurement of multiple cell markers. We detected Nb<sub>4</sub>C<sub>3</sub> in the <sup>93</sup>Nb channel and demonstrated its ability to be internalized by skin cells and its biocompatibility on the two skin cell models used, regardless of the extent of interactions. Our analysis detected Nb<sub>4</sub>C<sub>3</sub> in the <sup>93</sup>Nb channel, demonstrating its ability to be internalized by skin cells and confirming its biocompatibility across both skin cell models, regardless of the extent of interactions. Additionally, we employed reconstructed human epidermis tissue models (EpiDerm, EPI200) to evaluate potential irritation effects.

Our findings demonstrate that  $Nb_4C_3$  exhibits favorable uptake and maintains high cell viability across both cell types, while irritation assessments using the EpiSkin model indicated no adverse reactions. These results suggest that  $Nb_4C_3$  is a safe material with promising implications for cutaneous applications, supporting its potential use in dermatological products and therapies.

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