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## Biography

**Kelsey Retting**, PhD, is a scientific leader with over 15 years in drug development in biotechnology and pharmaceutical sectors. She earned her PhD in Biological Chemistry from UCLA. With expertise in cellular and molecular biology and in vitro pharmacology, Dr. Retting currently serves as a Senior Business Development Manager at QIMA Life Sciences, where she fosters drug development collaborations.

## Abrocitinib Impacts Memory T Cell Populations, Associated With Flare Recurrence In Atopic Dermatitis In Vitro And Ex Vivo

### Abstract:

Abrocitinib (abro), an FDA-approved JAK1 inhibitor, reduces clinical symptoms and flare frequency in atopic dermatitis (AD), yet its effects on memory T (TM) cells remain unclear. As TM cells are implicated in AD recurrence, we investigated abro's impact on circulating (CI-) and skin resident (R) TM cells in AD. PBMCs from eight AD patients were treated in vitro with vehicle or 5  $\mu$ M abro,  $\pm$   $\alpha$ CD3/ $\alpha$ CD28 stimulation. FACS demonstrated that while TCI-M cell numbers were unchanged, abro inhibited  $\alpha$ CD3/ $\alpha$ CD28-induced expansion of central and/or effector TCI-M cells, including CLA<sup>+</sup> skin-homing and CCR4<sup>+</sup> skin-tropic CD4<sup>+</sup> and CD8<sup>+</sup> subsets. To evaluate TRM cells, (peri-)lesional skin samples from 6-9 AD patients were cultured ex vivo with vehicle or 5  $\mu$ M abro. RNA-seq after 24 hours demonstrated that abro shifted the lesional transcriptome toward a peri-lesional-like state. After 48 hours, cytokine secretion of IL-6, IL-9, IL-24, and CCL17 trended downwards. Prolonged exposure (96 hours) resulted in significantly elevated GATA-3 protein levels in epidermal keratinocytes and a tendency toward filaggrin restoration in lesional samples, indicating improved barrier integrity. CD3<sup>+</sup>CD69<sup>+</sup>GATA3<sup>+</sup> TRM cell numbers were significantly higher in lesional epidermis and dermis than in peri-lesional tissue after 96 hours and remained unaffected by abro-treatment. Abro significantly or tendentially reduced epidermal CD3<sup>+</sup>CD45RO<sup>+</sup>CD69<sup>+</sup>, CD3<sup>+</sup>CD45RO<sup>+</sup>CLA<sup>+</sup>, and CD3<sup>+</sup>CD69<sup>+</sup>CD103<sup>+</sup> TRM cells in peri-lesional and/or lesional skin. 144 hours exposure also decreased CD3<sup>+</sup>CD45RO<sup>+</sup>CLA<sup>+</sup> TRM cells in lesional dermis. Our findings suggest that Abro limits expansion and persistence of TCI- and TRM cells, potentially contributing to reduced flare frequency and prevention of lesion extension in AD.