ABSTRACT

Keratinocyte differentiation and stratification bases epidermal morphogenesis and kept throughout life as tissue homeostasis and architecture is maintained. Yet, a considerable part of the molecular mechanisms that take place during stratification is still unexplored. Here we describe a novel role in integrin activating protein, kindlin, as promising regulator of keratinocyte stratification. The experimental evidence is shown through knockdown and overexpression of kindlin-1 or kindlin-2 and a double knockdown of kindlin-1 and kindlin-2. A time course analysis for quantification of RhoE and E-cadherin expression profile reveals the effect of kindlin-1 or kindlin-2 absences in establishing cell-cell contacts and stratification marker of RhoE transient upregulation upon induction of stratification in keratinocytes. We found RhoE transient upregulation is not achieved in the absence of kindlin-2 and a stark increase in stratifying cells is quantified in kindlin-2 overexpressing cells. Meanwhile, significant increase in E-cadherin expression is only achieved in kindlin-1 knockdown cells with significant difference in E-cadherin basal expression between kindlin-1 deficient and kindlin-2 deficient cells. Integrin activity was measured through quantification of adherent cells on collagen type IV coated plate. We discovered a distinct function of kindlin-1 and kindlin-2 in stratification, with kindlin-1 potentially regulating through E-cadherin expression while kindlin-2 via upstream upregulation of atypical small GTPase, RhoE.