

# Something's wrong in the cellular neighborhood

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Biological tissues and organs are typically surrounded by a boundary layer of cells known as an epithelium (or endothelium). When an epithelium is injured, surrounding cells respond in a distance-dependent manner to reseal the wound. So, how do the surrounding cells “know” that there is a wound nearby, i.e., that something is wrong in the cellular neighborhood? Across a wide range of organisms, the first response of epithelial cells to local wounds is a dramatic increase in cytosolic calcium. We have investigated this process in fruit flies using fast and reproducible laser wounds. Our results show that this increase occurs quickly – calcium floods into damaged cells within 15 milliseconds, moves into adjacent cells over  $\sim 20$  s, and appears in a much larger set of surrounding cells via a delayed second expansion over 40-300 s – but calcium is nonetheless a reporter: cells must detect wounds even earlier. We will discuss how measurements of laser-tissue interactions can be combined with quantitative image analysis and the genetic tools available in fruit flies to tease apart wound detection in terms of its physical and biochemical mechanisms. We will discuss the experimental evidence and a corresponding computational model developed to match experimental observations, test the plausibility of hypothesized mechanisms, and make experimentally testable predictions. This work supported by NIH Grant 1R01GM130130.