Investigating cellular and molecular mechanisms of ADP-heptose sensing and TIFAsomes dynamics in vivo using zebrafish

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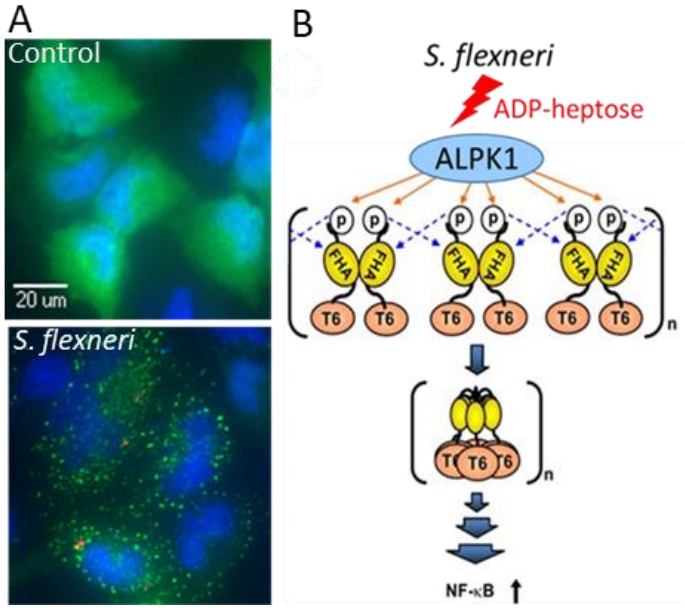
ADP-Heptose, an intermediate of LPS biosynthesis, is a newly discovered bacterial Pathogen-associated molecular pattern (PAMP). Upon binding to its receptor ALPK1, ADP-Heptose triggers a TIFA-dependent pro-inflammatory response. The recognition of ADP-heptose induces the formation of multi-protein structures called TIFAsomes, which, like inflammasomes, regulate innate immunity during infection *in vitro,* activating the transcription factor NF-κB and the secretion of inflammatory cytokines. The ALPK1/TIFA/TRAF6 axis activated in response to ADP-heptose recognition is a new pathway of innate immunity (Milivojevic et al 2017; Garcia-Weber et al, 2018). ADP-heptose is shared by most Gram-negative bacteria and thus by many important human pathogens, including *Shigella flexneri*, *Salmonella* Typhimurium and *Neisseria meningitidis*. Yet, the functional impact of ADP-heptose detection during bacterial infections *in vivo* is largely unknown. We are addressing the mechanisms of ADP-heptose sensing and the functional significance of TIFAsomes dynamics and activation in vivo, by using our *Shigella flexneri*-zebrafish infection model (Mostowy et al, 2013).



Mechanism of ADP-heptose sensing. **A**: Formation of TIFAsomes after Sf infection (TIFA in green, Sf in red, nuclei in blue). **B**: Diagram of TIFAsome formation (Cecile Arrieumerlou).