

No.	K25-3175	
Project Title	Crossroads between inflammasomes and adaptive immune responses	
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Joint Research Report (Annual/Project Completion)

Annual Report

Report (April 1, 2025-March 31, 2026)

Project title: “K25-3175: Crossroads between inflammasomes and adaptive immune responses”

One of the important immune signaling molecules we focused on recently is TANK-binding kinase 1 (TBK1), a famously known for its importance for anti-viral responses. Canonically, the recognition of viral nucleic acids by pattern-recognition receptors converges on TBK1 to initiate type I interferon responses and antiviral immunity. Beyond this canonical role, emerging evidence from genetic and pharmacological studies identifies TBK1 as a context-dependent regulator of both innate and adaptive immune responses (*Fischer et al, PNAS, 2021; Lee et al, J Exp. Medicine, 2022*). TBK1 exerts cell-type-specific functions that extend to the control of immune cell survival, differentiation, and effector activity. These expanded roles suggest that TBK1 is a central coordinator of immune function rather than a pathway-limited kinase. We further study on these non-canonical roles of TBK1 in different cell types and immune environments.

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1. Almeida MS, **Bezbradica J, Coban C**. TANK-binding kinase 1 (TBK1): Unexpected cell type-specific immune regulation beyond antiviral type I interferon signaling. **Invited Review, Current Opinion in Virology, 2026, in press.**
2. Lee MSJ, Inoue T, Ise W, Matsuo-Dapaah J, Wing JB, Temizoz B, Kobiyama K, Hayashi T, Patil A, Sakaguchi S, Simon AK, **Bezbradica JS**, Nagatoishi S, Tsumoto K, Inoue JI, Akira S, Kurosaki T, Ishii KJ, **Coban C**. B cell intrinsic TBK1 is essential for germinal center formation during infection and vaccination in mice. **Journal of Experimental Medicine, 2022**, Feb 7;219(2):e20211336. doi: 10.1084/jem.20211336.

Related Publication(s):

1. Fischer FA, Mies LFM, Nizami S, Pantazi E, Danielli S, Demarco B, Ohlmeyer M, Lee MSJ, **Coban C**, Kagan JC, Di Daniel E, **Bezbradica JS**. TBK1 and IKK ϵ act like an OFF switch to limit NLRP3 inflammasome pathway activation. **Proc Natl Acad Sci U S A. 2021**, September 21, 118 (38) e2009309118. doi.org/10.1073/pnas.2009309118. PMID: 34518217.