

NCGG SEMINAR

“FOXO and HSF-1 reverses immunosenescence in *C. elegans* via down-regulating insulin-like peptide endocrine signaling”

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Time and Date: at **15:30 ~ 16:30** on **21 Dec, 2018 (Fri)**

Room: The **2nd** floor Conference Hall Small
in the **1st** Research building, NCGG

<Reference for Seminar>

One of the hallmarks of aging is immunosenescence, a decline in immune functions, which appeared to be inevitable. Surprisingly, here we show that lifespan-extending DAF-2/insulin/IGF-1 receptor mutations drastically delay immunosenescence and even improve immunocompetence in old *C. elegans*. We showed that p38 mitogen activated protein kinase (PMK-1), a key determinant of immunosenescence in wild-type, was dispensable for this enhanced immunocompetence. We then found that INS-7/insulin-like peptide and ZIP-10/bZip transcription factor, which were up-regulated by aging in wild-type but not in *daf-2* mutants, contributed to immunosenescence. Moreover, we showed that longevity-promoting DAF-16/FOXO and heat-shock transcription factor 1 (HSF-1) increased immunocompetence in old *daf-2(-)* animals by decreasing the expression of *ins-7*, which in turn further down-regulated insulin/IGF-1 signaling. Our study suggests that reduced insulin/IGF-1 signaling can bypass normal immunosenescence via up-regulating anti-aging transcription factors that regulate an endocrine insulin-like peptide. Since insulin/IGF-1 signaling is evolutionarily conserved across species, the strategy for immune rejuvenation may be exploited for preventing immunosenescence in humans.

1. Lee, S.J.V. et al., Prefoldin 6 mediates longevity signaling from heat shock factor 1 to FOXO in *C. elegans*. *Genes Dev.* (Accepted)
2. Lee, S.J.V. et al, Reduced insulin/IGF-1 signaling promotes longevity via enhancing RNA surveillance in *C. elegans*. *Nat. Commun.* 8, 14749, (2017)
3. Lee, S.J.V. et al, Mitochondrial chaperone HSP-60 regulates anti-bacterial immunity via p38 MAP kinase signaling. *EMBO J.* 36(8): 1046-1065 (2017)

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