



האוניברסיטה העברית בירושלים
הפקולטה לחקלאות, מזון וסביבה ע"ש רוברט ה. סמית
המכון לביוכימיה, מדעי המזון והתזונה



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Title:

The prenyl binding protein PDL-1 regulates GLB-5 activity by targeting soluble guanylate cyclases to dendritic endings

המפגש יתקיים

ביום א', 11 ינואר 2015, בשעה 9:00

מועדון סגל

(1/11/2015, 9:00, Faculty Club)

Abstract:

Oxygen (O₂) is essential for the life of all aerobic animals. However, re-oxygenation of tissues after hypoxia triggers generation of reactive O₂ species (ROS) that may induce tissue damage. Animals must therefore not only monitor changes in O₂ and adapt to prolonged hypoxia, but also rapidly adjust their behavior, physiology, and cellular activity following reoxygenation. However, the sensing and adaptation mechanisms involved are not completely understood. The hexa-coordinated globin, GLB-5, tunes the dynamic range of *C. elegans* O₂-sensing neurons, enabling animals to switch behavior sharply in response to subtle changes in ambient O₂ levels. In the present study, we show that GLB-5 also enables fast behavioral and cellular recovery from hypoxia/reoxygenation (H/R) stress (Gross et al, 2014). We suggest that prolonged hypoxia reconfigures the threshold for O₂ responses in the O₂-sensing neurons URX and BAG, and that GLB-5 rapidly reconfigures the threshold to normoxic levels upon return to 21% O₂. Forward genetic screens indicate that the function of GLB-5 requires PDL-1, the *C. elegans* ortholog of mammalian PrBP/PDE6 δ protein. In mammals, PDE6 δ regulates the activity and traffic of prenylated proteins and non-prenylated Arf-like (Arl) small GTPases (Norton et al, 2005; Zhang et al, 2004). We show that PDL-1 targets the soluble guanylate cyclase O₂ sensors GCY-33 and GCY-35 to the dendritic endings of URX and BAG O₂-sensing neurons. At the dendritic ending, the soluble guanylate cyclases may be more exposed to O₂, and act together with GLB-5 to regulate fast recovery from H/R stress.

Gross E, Soltesz Z, Oda S, Zelmanovich V, Abergel Z, de Bono M (2014) GLOBIN-5-Dependent O₂ Responses Are Regulated by PDL-1/PrBP That Targets Prenylated Soluble Guanylate Cyclases to Dendritic Endings. *The Journal of neuroscience : the official journal of the Society for Neuroscience* **34**: 16726-16738
Norton AW, Hosier S, Terew JM, Li N, Dhingra A, Vardi N, Baehr W, Cote RH (2005) Evaluation of the 17-kDa prenyl-binding protein as a regulatory protein for phototransduction in retinal photoreceptors. *The Journal of biological chemistry* **280**: 1248-1256
Zhang H, Liu XH, Zhang K, Chen CK, Frederick JM, Prestwich GD, Baehr W (2004) Photoreceptor cGMP phosphodiesterase delta subunit (PDEdelta) functions as a prenyl-binding protein. *The Journal of biological chemistry* **279**: 407-413

סגל וסטודנטים מוזמנים להשתתף

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