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Royalactin induces queen differentiation in honeybees

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The honeybee (*Apis mellifera*) forms two female castes, the queen and the worker. This dimorphism depends not on genetic differences, but on ingestion of royal jelly (RJ). So far, I found that a 57-kDa protein in RJ, designated as royalactin, induces differentiation of honeybee larvae into queens. Royalactin increased body size and ovary development and shortened developmental time in honeybees. Surprisingly, it also showed similar effects in fruit fly (*Drosophila melanogaster*). Mechanistic studies revealed that royalactin activated p70 S6 kinase, which was responsible for the increase of body size, increased the activity of mitogen-activated protein kinase, which was involved in the decrease of developmental time, and increased the titer of juvenile hormone (JH), an essential hormone for ovary development. These actions were mediated by epidermal growth factor receptor (Egfr) in fat body (FB) of both insects, because knockdown of Egfr expression resulted in a defect of all phenotypes induced by royalactin. These findings indicated that a specific factor in RJ, royalactin, drives queen development through an Egfr-mediated signaling pathway. Furthermore, I investigated the factors involved in increase of fecundity by royalactin. I found that Egfr signaling in FB, which is activated by royalactin, leading to induction of JH synthesis and a consequent increase of yp expression, thereby increasing fecundity. Methoprene tolerant (Met) is a specific receptor of JH. The mutation of Met suppressed the increase of gene expression of yp and fecundity by RJ, but did not affect the changes of other phenotypes in flies reared with RJ. Inhibition of *Drosophila* Met in FB caused suppression of increased yp expression and fecundity in flies reared with RJ, suggesting that increase of JH titer by royalactin might induce upregulation of yp expression via Met in FB, leading to the increase of fecundity.