BIO230H -- Annotated Bibliography Yiyun Ding 1004705214 P5102C

Part1 Research Article 1

Full citation: Ma X, Wang H, Ji J, Xu W et al. Hippo Signaling Promotes JNK-dependent Cell Migration. PNAS 2017; 114: 1934-1939

The article discussed how Hippo pathway regulates the migration of Drosophila border cells. Migration of cells is important in the development of cellular environment but the mechanism of the Hippo pathway to promote cell migration remains unclear. Besides, actin cytoskeleton is known to be important for cell migration, so whether the cell migration regulation mechanism of Hippo pathway is actin cytoskeleton polarization was investigated. The hypothesis that the author made is that Hippo pathway can promote cell migration by polarizing the actin cytoskeleton in migrating border cell clusters. To identify the role of Hippo pathway, the authors inactivated Ex and Kib, which are upstream Hippo pathway components. Results showed that the inactivation delays border cell migration (Fig. 3, A-F). Besides, the authors studied the behavior of Hpo and Wts mutant clusters since Kib, Ex and Mer can activate the Hpo and Wts kinases. Results showed that F-actin didn't polarize but tended to accumulate throughout the cluster (Fig. 3, A-L), which indicated that if Hippo pathway activates Hpo and Wts, F-actin will be polarized, and the migration will be promoted. Therefore, this experiment supported the authors' hypothesis that Hippo pathway promotes border cell migration by polarizing the actin cytoskeleton. (Lucas et al., 2013)

Part1 Research Article 2

Full Citation: Lucas PE, Khanal I, Gaspar P, Fletcher CG, Polesello C et al. The Hippo Pathway Polarized the Actin Cytoskeleton during Collective Migration of Drosophila Border Cells. JCP 2013; 201: 875-885

The article discussed how Hippo pathway regulates the migration of Drosophila cells. Since the mechanism of Hippo signaling in cell invasion is still controversial, the authors want to elucidate

the Hippo pathway's contradictory roles. Since JNK is proven to modulate cell invasion, whether JNK signalling activation is the mechanism of Hippo pathway regulation in cell invasion is investigated. The hypothesis the authors made is that Hippo pathway activation induces JNK-dependent cell invasion through activating JNK signaling. First, to prove the hypothesis that Hippo pathway promote JNK-dependent cell migration, the authors overexpressed Hpo or Wts and found that the activated Hpo signaling triggered invasive migration and a significant number of GFP+ cells migrated away (Fig. 1 B'-D'). The result supported the hypothesis. Then, to prove that JNK signalling is required in cell invasion, the authors blocked JNK signaling and found that cell invasion behavior is impeded (Fig. 2E-J). Therefore, the authors argued that Hippo pathway can promote cell migration and activating JNK signaling is essential during cell migration, which supports the hypothesis (Ma et al., 2017)

Part 2

Cell migration is a central process in the development and maintenance of organism tissues. The progression of cancer is also tightly linked to it. Many researches show that Hippo pathway can promote cell migration. However, how hippo pathway regulate cell migration remains controversial. For example, Lucas et al. (2013) believe that Hippo pathway promote cell migration by polarizing the actin cytoskeleton without activating JNK signal (Fig. 3, A-L), while Ma et al. (2017) argued that JNK signal activation is essential for Hippo pathway to promote cell migration and cell migration will be impeded if JNK signalling is blocked (Fig. 2E-J). To elucidate Hippo pathway's contradictory roles in promoting cell migration, whether cell migration can be promoted by Hippo pathway when JNK signalling is blocked should be studied. The hypothesis is that Hippo pathway promote migration by polarizing the actin cytoskeleton and JNK signalling is not required.