Matrix Biology Highlights
Edited by Maria Gubbiotti and Tom Neill

1). Dlp/Mmp1 dysregulation is responsible for the synaptogenic defects characterized in fragile X syndrome.

Reference | Dear, M.L., Shilts, J., Broadie, K. 2017. Neuronal activity drives FMRP- and HSPG-dependent matrix metalloproteinase function required for rapid synaptogenesis. *Sci. Signal*. *10*, eaan3181.

The composition of the highly-specialized extracellular matrix found between synaptic partners is crucial for proper functioning and to further our understanding of disease processes. A recent study by Dear *et al,* and published in *Science Signaling,* reveals a novel interplay between Mmp1 and Dally like-protein (Dlp) in a fly model of fragile X syndrome (FXS). Using the Drosophila neuromuscular junction glutamatergic synapse as a model in the context of FXS, the authors found that rapid, activity-dependent synaptic ghost bouton formation required secreted Mmp1. Delving deeper, it was discovered that the HSPG glycan co-receptor Dlp was required for the accumulation of Mmp1, localization to the synapse, and the activity-dependent increase in Mmp1 (Fig. 1). Mechanistically, this increased abundance of Mmp1 relied on a physical interaction between Mmp1 and the heparan sulfate chains of Dlp. Applying these findings to the background of FXS, the authors reasoned that increased Dlp is responsible for the enhanced Mmp1 levels found in FXs. Therefore, loss of *dlp* (in parallel with loss of FMRP) was sufficient to restore homeostatic levels of Mmp1 and response to activity-dependent neural stimulation.

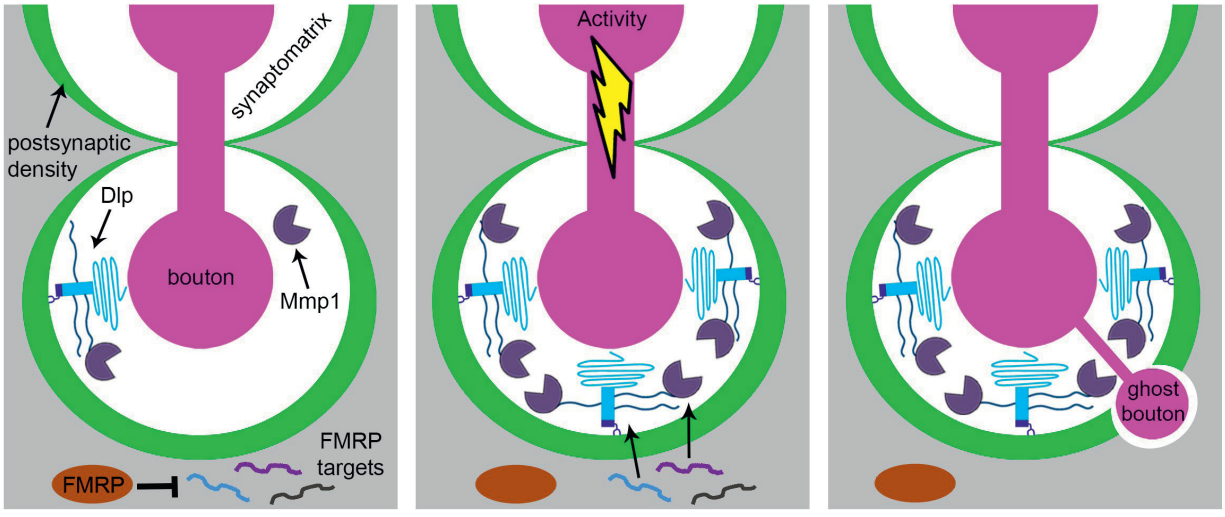

Figure 1. Schematic representation of activity-dependent Dlp/Mmp1 interactions required for ghost bouton formation. Figure kindly provided by Dear, M.L.

2). Deposition of basement membrane components, secreted by migrating macrophages, occurs in specific spatio-temporal patterns

Reference | Matsubayashi, Y., Louani, A., Dragu, A., Sanchez-Sanchez, B.J., Serna-Morales, E., Yolland, L., Gyoergy, A., Vizcay, G., Fleck, R.A., Heddleston, J.M., Chew, T.-L., Siekhaus, D.E., Stramer, B.M. 2017. A moving source of matrix components is essential for de novo basement membrane formation. *Current Biol. 27*, 3526-3534.

Nearly all epithelial cells reside on a thin, but critical, layer of extracellular matrix commonly known as the basement membrane (BM). Despite the evolutionarily conserved nature of the BM, both in architecture and composition, the question of where and when the individual pieces are generated then subsequently organized to give rise to a mature BM lingers. In a recently published article in *Current Biology,* Matsubayashi and colleagues combined sophisticated microscopy techniques with genetic approaches to reveal the dynamics of this fundamental structure. Their findings revealed a sequential and temporal hierarchy of BM protein synthesis (Fig. 2A) and component deposition (Fig. 2B) that underlies BM maturation during *Drosophila* embryogenesis. The authors then demonstrated that a specific subpopulation of BM proteins (e.g. collagen IV) must be secreted by migrating hemocytes for even distribution throughout the embryo (Fig. 2C,D) This study underscores and broadens the importance of mammalian macrophages in the construction of BM.

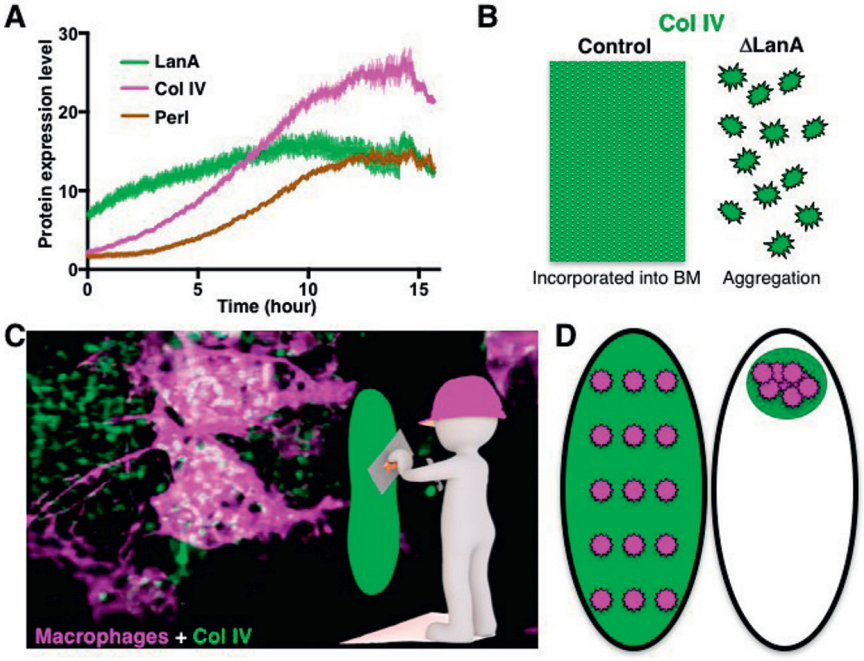

Figure 2. BM components are temporally synthesized and deposited by macrophages during embryogenesis. (A) Temporal expression profiles of BM components during *Drosophila* embryogenesis. Laminin A (LanA) is expressed first, followed by Collagen IV (Col IV) and then Perlecan (Perl). (B) Functional importance of the temporal hierarchy of BM component expression. LanA is expressed earlier than Col IV; in the absence of LanA, Col IV aggregates. (C) Macrophages (magenta) locally 'plasters' Col IV (green) they produce. (D) Macrophages (magenta) originate embryo's head then evenly disperse throughout the body. When dispersal fails and macrophages remain in the head, Col IV (green) is deposited only around the stuck macrophages. Figure kindly provided by Matsubayashi, Y.