Resolving the Building Blocks and Self-Assembly Principles of Cell-Matrix Adhesion Sites

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Abstract

How can the integrin adhesome get self-assembled locally, rapidly, and correctly as diverse cell-matrix adhesion sites? In order to address this question we monitored the integrin adhesome protein network in individual adhesion sites and in the cytosol. Using fluorescence cross-correlation spectroscopy and fluorescence recovery after photobleaching we found that the integrin adhesome is extensively pre-assembled in the cytosol, forming multi-protein building blocks for adhesion sites. These building blocks are combinatorially diversified, confined in their size and correlate with the structural and functional organization of proteins across focal adhesions. We also found that stationary focal adhesions release symmetrically the same types of protein complexes that they recruit, thereby keeping the cytosolic pool of building blocks spatiotemporally uniform. Based on these results we concluded a model in which multi-protein building blocks enable rapid and modular self-assembly of adhesion sites and symmetric exchange of these building blocks preserves their specifications and thus the assembly logic of the system. To explore this assembly logic, we have established a high-throughput toponome imaging of intracellular proteins, enabling to co-image a large number of proteins and their phosphorylation states in many individual adhesion sites following live cell imaging. Multi-dimensional analyses of the obtained toponome data indicate high-order statistical relations between the local levels of the components, thereby revealing system-level principles of focal adhesions assembly.