## Coalescent angiogenesis—evidence for a novel concept of vascular network maturation

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Angiogenesis describes the formation of new blood vessels from pre-existing vascular structures. While the most studied mode of angiogenesis is vascular sprouting, specific conditions or organs favor intussusception, i.e., the division or splitting of an existing vessel, as preferential mode of new vessel formation. In the present study, sustained (33 h) intravital microscopic observation of the vasculature in the chick chorioallantoic membrane (CAM) led to the recognition of a novel non-sprouting mode for vessel generation, which we termed "coalescent angiogenesis." In this process, preferential flow pathways evolve from isotropic capillary meshes enclosing tissue islands. These preferential flow pathways progressively enlarge by coalescence of capillaries and elimination of internal tissue pillars, in a process that is the reverse of classic intussusception. Concomitantly, less perfused segments regress. In this way, an initially mesh-like capillary network is remodeled into a tree structure, while conserving vascular wall components and maintaining blood flow. Coalescent angiogenesis, thus, describes the remodeling of an initial, hemodynamically inefficient mesh structure, into a hierarchical tree structure that provides efficient convective transport, allowing for the rapid expansion of the vasculature with maintained blood supply and function during development.

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