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Title: Shape self-regulation during lung development

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Body: The bronchial tree results from the self-avoiding branching of lung epithelium in the mesenchyme. While the molecular basis of morphogenesis has been extensively studied, the individual branching mechanism and the organ-scale organization process remain unclear. We designed an innovative biophysical model of lung development. We found that the diffusion of the major growth factor (FGF10) from distal mesenchyme where Fgf10 is known to be expressed accounts for the patterning of FGF10 downstream targets (Fig. 1).

We then developed 2D and 3D development simulations. Starting from a unique epithelial tube, and calculating local epithelial growth as a function of FGF10 reception, we found that most of the striking features of lung geometry - self-avoiding and space-filling branching, asymmetry, size dispersion, etc - emerge spontaneously through mechanisms that we detail (Fig. 2).

Our results suggest that self-organization may play a major role in lung branching morphogenesis. They provide a direct link between genotype, phenotype, and phenotypic variability. They are consistent with morphometric data and with mutant phenotypes. Finally, they question the well-accepted scenario of a master genetic routine.