

## Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: Predicted regulatory heterogeneities in 3D-cultured B2B1 cells minus AP heterodimerizer.

File Name: Supplementary Data 2

Description: Predicted regulatory heterogeneities in 3D-cultured B2B1 cells plus AP heterodimerizer.

File Name: Supplementary Data 3

Description: Transcript heterogeneities and estimated expression frequencies for high-priority targets and candidates for the DE phenotype.

File Name: Supplementary Data 4

Description: Initial conditions and rate constants for the systems model of nucleocytoplasmic transport.

File Name: Supplementary Data 5

Description: Proximity labeled proteins in B2B1 cells expressing BirA\*-CSE1L or BirA\*-NUP37.

File Name: Supplementary Data 6

Description: Genomic loci bound by chimeric EGFR in B2B1 cells with or without AP heterodimerizer.

File Name: Supplementary Data 7

Description: Cloning details, PCR primers, and antibodies.

File Name: Supplementary Movie 1

Description: Brightfield time lapse of B2B1 outgrowths treated with AP heterodimerizer for the indicated times. Scale bar is 100  $\mu\text{m}$ .