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**Supplementary information**

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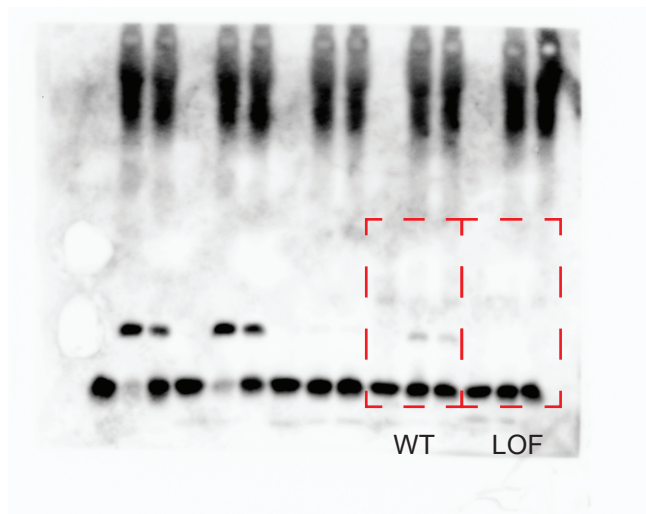
**Affinity-optimizing enhancer variants  
disrupt development**

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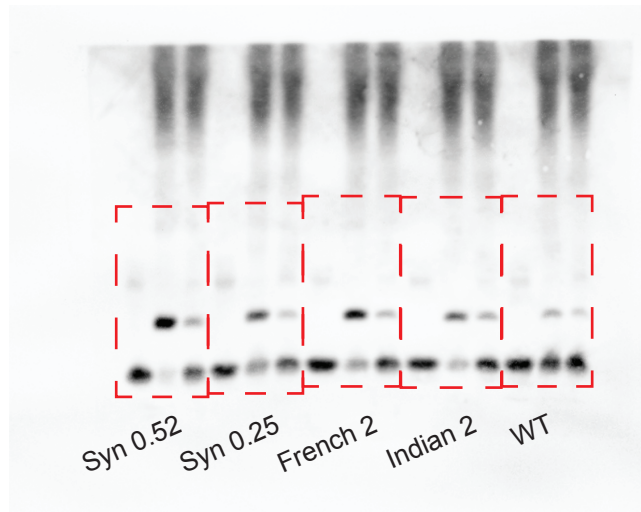
In the format provided by the  
authors and unedited

# Supplementary Information Figure 1

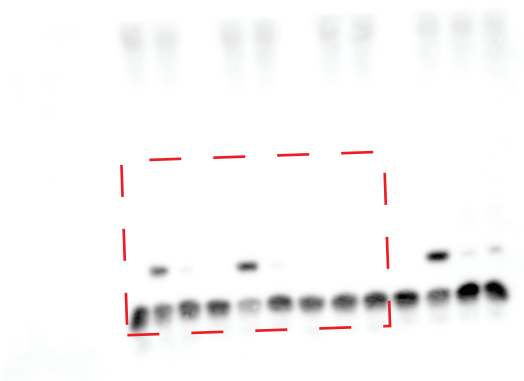
**A** ETS-1 binding to ETS-A site in ZRS  
(Extended Data Figure 4A)



**B** ETS-1 binding to ETS-A site in ZRS  
(Extended Data Figure 4B)



**C** HOXA13 binding to Dutch 2 variant in ZRS  
(Extended Data Figure 8A)



**D** HOXD13 binding to Dutch 2 variant in ZRS  
(Extended Data Figure 8B)

