

minimum, experimental studies of multiple BDCPs together will be necessary to test the *in silico* predictions that they bind to each other. With more BDCP functional data emerging, possible targets for therapy, including modification of autophagy, can be evaluated for the increasing number of BDCP-related human diseases.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Figure S1: Phylogenetic tree of human BDCPs in diagonal format. This tree was created by comparing the BEACH domain regions from each BDCP, as annotated in Entrez. WRD81 is the most divergent followed by NSMAF. LRBA and NBEA, NBEAL1 and NBEAL2, and LYST, WDFY3 and WDFY4 are most like each other. The scale bar represents a degree of divergence 0.1, as is typically shown for phylogenetic trees.

REFERENCES

1. Ponting CP, Russell RR. The natural history of protein domains. *Annu Rev Biophys Biomol Struct* 2002;31:45-71.
2. Nagle DL, Karim MA, Woolf EA, Holmgren L, Bork P, Misumi DJ, McGrail SH, Dussault BJ Jr, Perou CM, Boissy RE, Duyk GM, Spritz RA, Moore KJ. Identification and mutation analysis of the complete gene for Chediak-Higashi syndrome. *Nat Genet* 1996;14:307-311.
3. Barbosa MD, Nguyen QA, Tchernev VT, Ashley JA, Detter JC, Blaydes SM, Brandt SJ, Chotai D, Hodgman C, Solari RCE, Lovett M, Kingsmore SF. Identification of the homologous beige and Chediak-Higashi syndrome genes. *Nature* 1996;382:262-265.
4. Perou CM, Moore KJ, Nagle DL, Misumi DJ, Woolf EA, McGrail SH, Holmgren L, Brody TH, Dussault BJ Jr, Monroe CA, Duyk GM, Pryor RJ, Li L, Justice MJ, Kaplan J. Identification of the murine beige gene by YAC complementation and positional cloning. *Nat Genet* 1996;13:303-308.
5. Wang J-W, Gamsby JJ, Highfill SL, Mora LB, Bloom GC, Yeatman TJ, Pan TC, Ramne AL, Chodosh LA, Cress WD, Chen J, Kerr WG. Deregulated expression of LRBA facilitates cancer cell growth. *Oncogene* 2004;23:4089-4097.
6. Lopez-Herrera G, Tampella G, Pan-Hammarström Q, Herholz P, Trujillo-Vargas CM, Phadwal K, Simon AK, Moutschen M, Etzioni A, Mory A, Srugo I, Melamed D, Hultenby K, Liu C, Baronio M, et al. Deleterious mutations in LRBA are associated with a novel syndrome of immune deficiency and autoimmunity. *Am J Hum Genet* 2012;90:986-1001.
7. Castermans D, Wilquet V, Parthoens E, Huysmans C, Steyaert J, Swinnen L, Fryns JP, Van de Ven W, Devriendt K. The neurobeachin gene is disrupted by a translocation in a patient with idiopathic autism. *J Med Genet* 2003;40:352-356.
8. Chen J, Lu Y, Xu J, Huang Y, Cheng H, Hu G, Luo C, Lou M, Cao G, Xie Y, Ying K. Identification and characterization of NBEAL1, a novel human neurobeachin-like 1 protein gene from fetal brain, which is up regulated in glioma. *Mol Brain Res* 2004;125:147-155.
9. Gunay-Aygun M, Falik-Zaccai TC, Vilboux T, Zivony-Elboun Y, Gumruk F, Cetin M, Khayat M, Boerkoel CF, Kfir N, Huang Y, Maynard D, Dorward H, Berger K, Kleita R, Anikster Y, et al. NBEAL2 is mutated in gray platelet syndrome and is required for biogenesis of platelet α -granules. *Nat Genet* 2011;43:732-734.
10. Albers CA, Cvejic A, Favier R, Bouwmans EE, Alessi M-C, Bertone P, Jordan G, Kettleborough RNW, Kiddle G, Kostadima M, Read RJ, Sipos B, Sivapalaratnam S, Smthurst PA, Stephens J, et al. Exome sequencing identifies NBEAL2 as the causative gene for gray platelet syndrome. *Nat Genet* 2011;43:735-737.
11. Kahr WHA, Hinckley J, Li L, Schwertz H, Christensen H, Rowley JW, Pluthero FG, Urban D, Fabbro S, Nixon B, Gadzinski R, Storck M, Wang K, Ryu G-Y, Jobe SM, et al. Mutations in NBEAL2 encoding a BEACH protein, cause gray platelet syndrome. *Nat Genet* 2011;43:738-740.
12. Zhao H, Yang W, Qiu R, Li J, Xin Q, Wang X, Feng Y, Shan S, Liu Y, Gong Y, Liu Q. An intronic variant associated with lupus erythematosus changes the binding affinity of Yingyang1 to downregulate WDFY4. *Genes Immun* 2012;13:536-542.
13. Gulsuner S, Tekinay AB, Doerschner K, Boyaci H, Bilguvar K, Unal H, Ors A, Onat OE, Atalar E, Basak AN, Topaloglu H, Kansu T, Tan M, Tan U, Gunel M, et al. Homozygosity mapping and targeted genomic sequencing reveal the gene responsible for

Figure S1:

