

Reply to Brunet and Doolittle: Both selected effect and causal role elements can influence human biology and disease

We agree with Brunet and Doolittle (1) on the utility of distinguishing the evolutionarily selected effects (SE) of some genomic elements from the causal roles (CR) of other elements that lack signatures of selection (1–4). DNA sequences identified by biochemical approaches include both SE and CR elements, and genetic variation in both has been implicated in human traits and disease susceptibility. We thus view the Encyclopedia of DNA Elements (ENCODE) catalog and similar data resources as important foundations for understanding the DNA elements and molecular mechanisms underlying human biology and disease.

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1 Brunet TDP, Doolittle WF (2014) Getting “function” right. *Proc Natl Acad Sci USA* 111:E3365.

2 Kellis M, et al. (2014) Defining functional DNA elements in the human genome. *Proc Natl Acad Sci USA* 111(17): 6131–6138.

3 Germain PL, Ratti E, Boem F (2014) Junk or functional DNA? ENCODE and the function controversy. *Biol Philos*, 10.1007/s10539-014-9441-3.

4 Doolittle WF, Brunet TDP, Linquist S, Gregory TR (2014) Distinguishing between “function” and “effect” in genome biology. *Genome Biol Evol* 6(5):1234–1237.

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The authors declare no conflict of interest.

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