

Supplementary information to: Don't discount all curcumin trial data

Supplementary references and the full list of signatories to a Correspondence published in *Nature* **543**, 40 (2017);

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We argue that the clinical potential of the spice extract curcumin should not be dismissed simply on the grounds that it yields confusing results in molecular drug screens (*Nature* **541**, 144–145; 2017; see also K. M. Nelson *et al.* *J. Med. Chem.* <http://doi.org/bw46>; 2017).

Nelson and colleagues claim a lack of evidence for curcumin's therapeutic benefits "despite thousands of research papers and more than 120 clinical trials" (www.clinicaltrials.gov). However, a PubMed search under 'curcumin double-blind placebo-controlled clinical trial' yields 49 entries, of which 17 recent trials show efficacy^{1–17}. In addition, there are 27 other clinical trials (for example, refs 18–24) and at least 5 animal studies of curcumin that point to therapeutic benefits (for example, refs 25–28).

The assumption that a drug candidate must have a single known target and compatibility with high-throughput screening to enter the clinic can preclude promising drug candidates (R. L. Elliott *Am. Chem. Soc. Med. Chem. Lett.* **3**, 688–690; 2012). Current detection methods for target engagement cannot gauge the full pharmacological spectrum of an investigational drug, so should be used with other screening paradigms. Also, the binding behaviour of curcumin to multiple molecular targets is associated with modulation rather than outright inhibition^{29,30}. And high-throughput screening is prone to technical artefacts that can make it a deceptive arbiter for excluding potential drugs.

In light of these considerations, curcumin's molecular targets and their regulatory mechanisms warrant further investigation if we are to build on the promising results that are already to hand in humans and animals.

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