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A protein kinase switch

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Kinase inhibitors are plagued by a lack of specificity. Now in the 21 September Nature Bishop *et al*. tackle the problem by building on their earlier work, in which they modified the ATP-binding sites of Src-family tyrosine kinases to accept either nucleotide analogs or modified kinase inhibitors. In the new work the researchers mutate kinases from four distinct kinase families by replacing a bulky residue with a small residue. This change provides enough room for the binding of inhibitor analogs, which are larger than their parent inhibitors and thus do not inhibit wild-type kinases (*Nature* 2000, **407**:395-401). The *in vivo* specificity is demonstrated using expression arrays. Most kinases contain a bulky residue analogous to the one mutated in this study, and thus should be amenable to the kinase-sensitization strategy.

References

1. Exploiting chemical libraries, structure, and genomics in the search for kinase inhibitors.

2. Nature, [http://www.nature.com/nature/]

3. Engineering Src family protein kinases with unnatural nucleotide specificity.