Supplementary Figure 1
Effect of the SH2-N-lobe interaction on Abl activity after pre-phoshorylation by Hck
Kinase activities of the pre-phosphorylated KD, SH2-KD, and two mutated variants thereof referenced to the activity of the isolated, unphosphorylated kinase domain (see Figure 2). Pre-incubation with Hck does not significantly enhance the activity of the isolated kinase domain, but slightly increases the activities of the three SH2-KD constructs (by a maximum factor of ~ 1.7). The relative activities of the pre-phosphorylated constructs are similar to what was seen without pre-phosphorylation (Figure 2). Perturbation of the SH2-N-lobe interface by the mutation I164E reduces the stimulating effect of the SH2 domain, while the mutation T231R enhances it.

Supplementary Figure 2
Detail of the active site in the crystal structure of the SH2-KD construct with dasatinib
Cartoon representation of the active site in the crystal structure of the SH2-KD construct (chain B, grey) in complex with dasatinib (cyan, ball-and-stick representation). The DFG motif is colored orange and shown in ball-and–stick representation. The Fo-Fc omit electron density (contoured at 3.0 σ) for the DFG motif and dasatinib is shown.

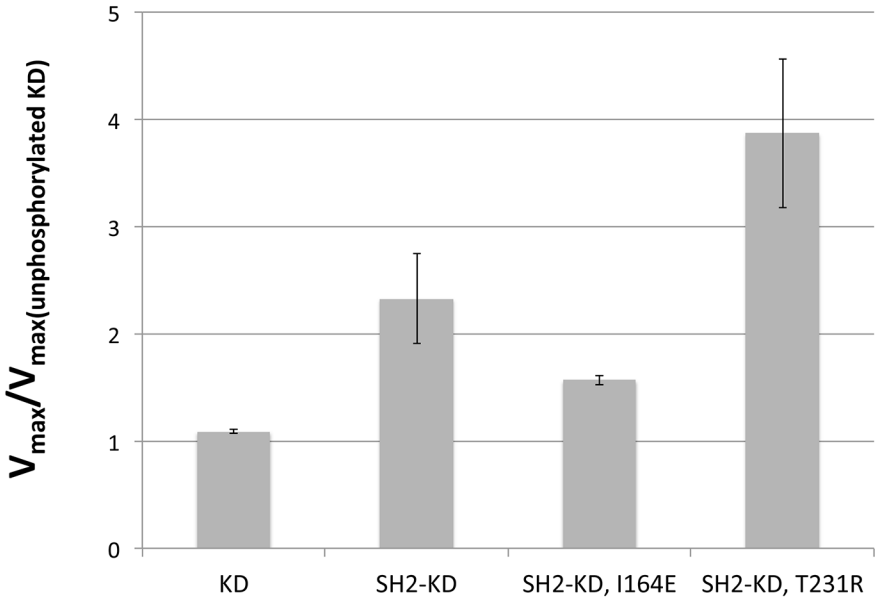
Supplementary Figure 3
Model of how Abl dimerization might promote processive substrate phosphorylation
(A) Two peptides were modeled onto the structure of the Abl dimer observed in our crystal: A phosphotyrosine-containing peptide was modeled onto the SH2 domain of Abl subunit II based on the crystal structure of a peptide-bound SH2 domain of Src (PDB ID: 1SPS) [1]. The substrate peptide bound to the active site of Abl subunit I was modeled based on a crystal structure of the kinase domain with an ATP-peptide conjugate (PDB ID: 2G2I) [2]. In our model the two peptides have the same directionality and could, in principle, represent two parts of a substrate with multiple tyrosine residues that spanning across the dimer interface.
(B) Detail of the crystallographic dimer interface shown in (A). The interface is centered on a key aromatic stacking interaction between Tyr 158 of the SH2 domain of subunit II (yellow) and Tyr 468 in helix αC of the C-lobe of subunit I (light blue).

Supplementary references

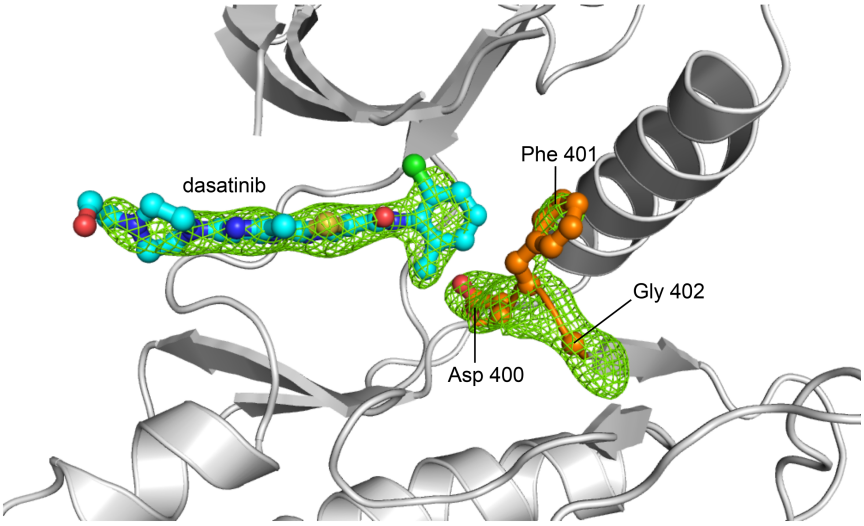
1 Waksman, G., Shoelson, S. E., Pant, N., Cowburn, D. and Kuriyan, J. (1993) Binding of a high affinity phosphotyrosyl peptide to the Src SH2 domain: crystal structures of the complexed and peptide-free forms. Cell **72**, 779–790.
2 Levinson, N. M., Kuchment, O., Shen, K., Young, M. A., Koldobskiy, M., Karplus, M., Cole, P. A. and Kuriyan, J. (2006) A Src-like inactive conformation in the abl tyrosine kinase domain. PLoS Biol. **4**, e144.

SUPPLEMENTARY FIGURES

Supplementary figure 1

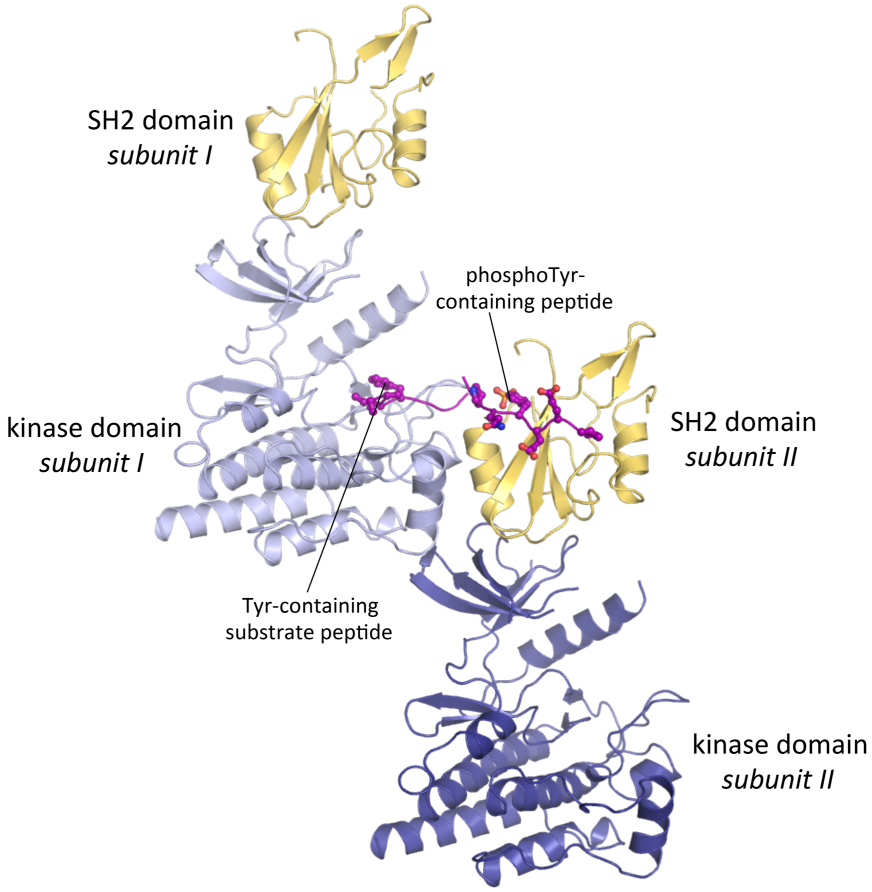


Supplementary figure 2



Supplementary figure 3

(A)



(B)