



Figure S1

Class-distinctive sites in structural context.  $G\alpha$ 1 is in complex with the  $G\beta\cdot G\gamma$  (deepblue/copper cartoon) heterodimer (PDB ID 1GP2).  $G\alpha$  is shown as spheres (A) or cartoon (B) with core residues colored gray if the residues are conserved between  $G\alpha$  subunits of different classes. All distinctive sites are colored according to the distinctive class ( $G(io)$  = green;  $G(q)$  = hot pink;  $G(s)$  = marine;  $G(12)$  = yellow orange). Non-core residues and d sites are colored white. Class-distinctive sites are numbered according to their position in the signature sequence (see Figures 4D, 5D, 6D, 7D, 8). Sites are placed on  $G\alpha$ 1 for relative positioning, no actual mammalian  $G\alpha$  subunit has distinctive sites from more than one class unless it is a chimera.