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Oral presentation

A molecular view of the regulation of sGC activity

Michael A Marletta*[1,2], Emily R Derbyshire[2], W Kaya Erbil[1], Nathaniel B Fernhoff[2], John Kuriyan[1,2], Charles Olea Jr[2], Mark S Price[2] and David E Wemmer[1]

Address: [1]Department of Chemistry, University of California, Berkeley, California 94720-3220, USA and [2]Department of Molecular and Cell Biology, University of California, Berkeley, California 94720-3220, USA

Email: Michael A Marletta* - marletta@berkeley.edu

* Corresponding author

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Mammalian sGC is a heterodimer composed of α- and β-subunits (Figure 1). The C-terminus of each subunit contains a catalytic domain and the active site is composed of residues from both subunits. The catalytic domains also form a pseudosymmetric active site that contains residues known to be involved in nucleotide binding, but lack the amino acids required for catalysis. Sequence analysis shows that each subunit also contains well-defined PAS-like domain, and a predicted helical region. The N-termini of the α- and β-subunits are homologous to the H-NOX (Heme-Nitric oxide/OXygen) family of proteins. The N-terminus of β-subunit contains a ferrous heme cofactor that serves a receptor for NO. sGC activity is also modulated by ATP and the substrate GTP and recent studies point toward a more complicated role for NO in the regulation of activity. Structural results coupled with biochemical and cellular experiments have broadened the current molecular view of the regulation of sGC.

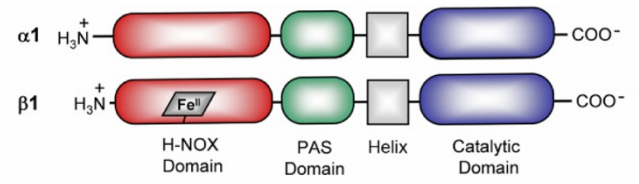

Figure 1
Domain structure of sGC.