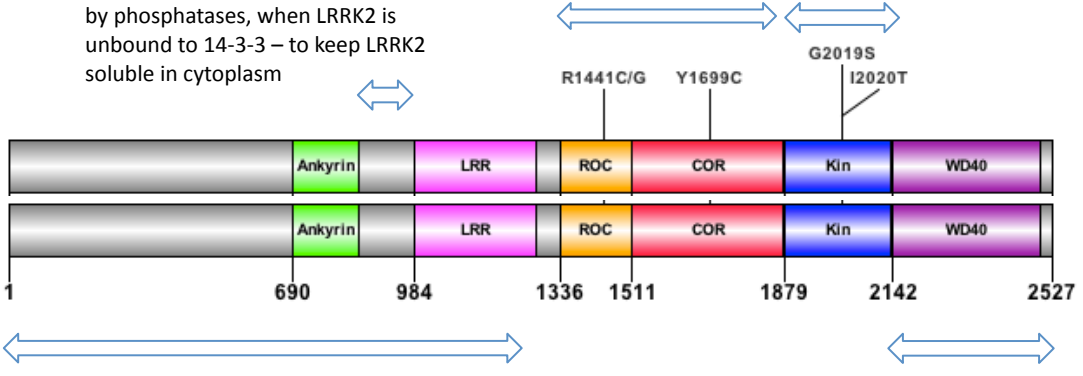
(A) Inhibition of kinase activity and GTP binding

1. Direct inhibition using ATP inhibitors on kinase domain – to attenuate kinase induced toxicity
2. Peptide blocking of the GTP binding pocket of ROC – to prevent any conformational change of LRRK2 upon GTP binding that may be associated with recruitment of mediators of cytotoxicity

(D) Preservation of constitutive phosphorylation of LRRK2

1. Peptide 'capping' to protect these phosphosites from dephosphorylation by phosphatases, when LRRK2 is unbound to 14-3-3 – to keep LRRK2 soluble in cytoplasm



(B) Disruption of LRRK2 dimerization

1. Peptide inhibition to interfere with dimer formation – to cause loss of kinase function

(C) Interference of protein-protein interaction platform

1. Peptide inhibition to block binding of proteins involved in mediating cytotoxicity

(C)