Oligomeric interfaces in transmembrane proteins: an analysis

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Thanks to the increasing amount of transmembrane protein (TM) structures being solved, it is now possible to carry out extensive studies of oligomeric interfaces in the transmembrane region. We have compiled the first fully comprehensive dataset of validated transmembrane protein interfaces (TMPBio) in order to study their features and assess what differentiates them from their soluble counterparts [1]. The general features of interfaces in the TMPBio set do not differ much from those of soluble proteins: they are large, tightly packed and possess many interface core residues. Notably, membrane lipids were not found to significantly mediate interfaces in TMPBio. We also used the dataset to validate the performance of our Evolutionary Protein Protein Interface Classifier (www.eppic-web.org) [2], developed on soluble protein data, on membrane proteins and found it to be about 80%. Although no G protein-coupled receptor (GPCR) was included in the validated set, we analyzed the crystallographic dimerization interfaces proposed in the literature. We found that the putative dimer interfaces proposed for class A GPCRs do not show the usual patterns of stable biological interfaces, neither in terms of evolution nor of packing, thus they likely correspond to crystal interfaces. We cannot however rule out the possibility that they constitute transient or weak interfaces. In contrast we do observe a clear biological interface signature for the proposed dimer of the class F human Smoothened receptor [3].

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[2] J.M. Duarte, A. Srebniak, M.A. Schärer, G. Capitani, *BMC Bioinformatics*, **2012**, *13*, 334.
[3] C. Wang *et al*, *Science*, **2013**, *497*, 338–343.