**Table 2 Properties of disorder in C1CRs**

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| --- | --- |
| **IDP characteristic** | **Key descriptors for C1CR ICDs** |
| Specific amino acid composition | The C1CR-ICDs have a unique amino acid composition that distinguishes them from both folded proteins and IDPs. *Depleted* in Met, Arg, Ala, and Lys compared to folded proteins and IDPs *Enriched* in Cys, Trp, Leu and Val compared to IDPs *Highly enriched* in Pro compared to folded proteins and IDPs |
| Disordered | All the ICDs of the C1CRs are predicted disordered throughout their sequences, but has been shown experimentally only for the GHR and PRLR |
| Rich in SLiMs | #Several SLiMs are common to groups of the C1CRs, in particular * BOX1 motifs (JAK/SH2)

 ΦΦP.ΦP.P (JAK2) ΦP.P (JAK1) ΦΦP.ΦP.[P/Φ].[P/Φ](JAK3/TYK2)* 14-3-3

 R[^DE](0,2)[^DEPG][ST][^PRIKGN]-P R[^DE](0,2)[^DEPG][ST][^P]\** SOCS2/3

 pY[AFILVWY].[AFILVWY](loose SH2-motif)* PDZ ..[ST].[ACVILF]\* (Class 1)

 ..[VLIFY].[ACVILF]\* (Class 2) ..[DE].[ACVILF]\* (Class 3)* TRAF2/6

 [PSAT].[QE]E (TRAF2) [P].[Q]..D (TRAF2) [P].[Q]..[FYWHDE] (TRAF6)* STAT

 [Y]..[P] (STAT1) [Y]..[Q] (STAT3) [Y][VLTFIC].. (STAT5) (promiscuous) [Y]..[F] (STAT6)* Phospho-degrons

 D[S]G.(2,3[ST] [LIVMP].(0,2)(T)P..[ST]* Dileucine motifs

 [D/E]...[L/I] [D/E]..LL* Tyrosine-based internalization motifs

 Y..[LMVIF]Only very few SLiMs have been addressed experimentally and only 7 three-dimensional structures exist of complexes. |
| Rich in PTMs | All C1CR-ICDs have numerous predicted phosphorylation sites distributed along the chain, but only few have been confirmed by MS or by mutational studies. Some SLiMs are regulated by phosphorylation |
| Alternative splice variants | Out of a total of 29 C1CRs, 16 have at least two isoforms differing in their ICDs, but up to five ICD isoforms are seen for some receptors (PRLR, IL-31R).Isoforms allow for network rewiring by insertion and deletion of specific SLiMs |
| Dynamic conformational ensemble | The CIDER analysis and measured *Rg* of presentative C1CR-ICDs suggest that they take on a slightly compacted, but dynamic ensemble |
| Multispecificity | Overlapping SLiMs dominates C1CR-ICDs and allow competition as a regulatory mechanism. This is made possible as the disordered chain can adapts to several different binding partner. |

#:^means that it cannot be a residue of this kind; \* indicates the negatively charged C-terminal; For the JAK binding motifs, the similar PXP motif is shaded in grey. Φ illustrate ant hydrophobic residue.