# The H3 loop of antibodies shows unique structural characteristics.

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3D modelling of antibodies is an important problem. Five of the six CDR loops that form the combining site are generally fairly easy to model since they generally adopt so-called canonical conformations, which can be predicted using sequence-based rules. However, these rules do not apply to CDR-H3, which has extremely high variability in both sequence and length (from 2 residues to over 30). This extreme variability arises from the V-D-J splicing that occurs at the DNA level to generate antibodies. Unfortunately, CDR-H3 is situated centrally within the antibody combining site making it the dominant CDR in many antigen interactions, making it very difficult to produce useful models, particularly with longer CDR-H3s.

In this paper, Regep *et al.* compare the structures of CDR-H3 loops with loops from non-antibody structures. They find that over 75% of CDR-H3 loops do not have near structural neighbours in other proteins. Comparing non-redundant protein fragments, over 30% of CDR-H3 loops are unique in structure compared with less than 3% of non-antibody loops.

This paper is important because it impacts on approaches to modelling CDR-H3. In general, protein loop modelling methods are either '*ab initio*' (somehow generating a conformation computationally) or 'knowledge-based' (using fragments from other proteins). These findings suggest that knowledge-based approaches that use loops from unrelated proteins are likely to be less effective than when these types of approaches are applied to other protein families.

**Disclosures**
None declared