

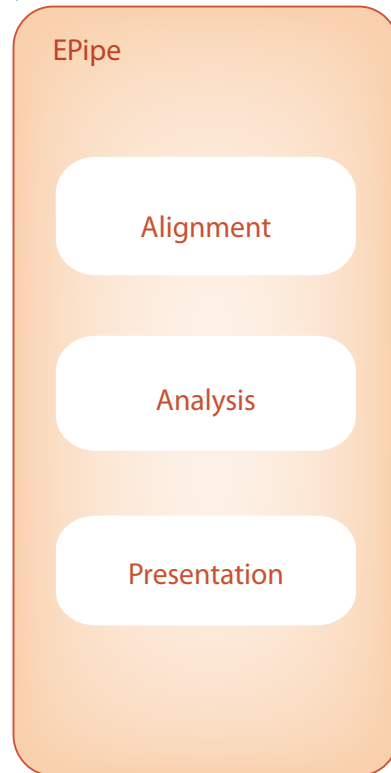
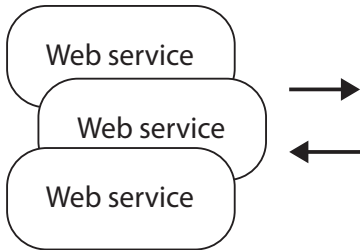
Input

Four isoforms of IFN receptor

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>AP000295.6-001
MLLSQNAFIFRSLNLVLMVYISLVFGISYDSPDYDESCTFKISLRNFRSILSWELKNHS
IVPTHYTLTYTMSKPEDLKVKNKNCANTRSFCDLTDEWRSTHEAYVTVLEGFSGNTTLF
SCSHNFWLAIDMSFEPPEFEIVGFTNHINVMVKFSPSIVEEELQFDLSLVIEEQSEGIVVK
HKPEIKGNMMSGNFYIIDKLPNTNYCVSVYLEHSDEQAVIKSPLKCTLLPPGQSESAE
SAKGGIITVFLIALVLTSTVTLKMGYICLRNSLPKVLRRGLAKGWNVAIHRCSHNA
LQSETPELKGSSCLSPSSWDYKRALCP9D
>AP000295.6-003
MLLSQNAFIFRSLNLVLMVYISLVFGISYDSPDYDESCTFKISLRNFRSILSWELKNHS
IVPTHYTLTYTMSKPEDLKVKNKNCANTRSFCDLTDEWRSTHEAYVTVLEGFSGNTTLF
SCSHNFWLAIDMSFEPPEFEIVGFTNHINVMVKFSPSIVEEELQFDLSLVIEEQSEGIVVK
HKPEIKGNMMSGNFYIIDKLPNTNYCVSVYLEHSDEQAVIKSPLKCTLLPPGQSESEFS
>AP000295.6-007
MEHKPEIKGNMMSGNFYIIDKLPNTNYCVSVYLEHSDEQAVIKSPLKCTLLPPGQSESE
AESAKGGIITVFLIALVLTSTVTLKMGYICLRNSLPKVLRRGLAKGWNVAIHRCSH
NALQSETPELKGSSCLSPSSWDYKRALCP9D
>AP000295.6-008
MLLSQNAFIFRSLNLVLMVYISLVFGISYDSPDYDESCTFKISLRNFRSILSWELKNHS
IVPTHYTLTYTMSKPEDLKVKNKNCANTRSFCDLTDEWRSTHEAYVTVLEGFSGNTTLF
SCSHNFWLAIDMSFEPPEFEIVGFTNHINVMVKFSPSIVEEELQFDLSLVIEEQSEGIVVK

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Output

Feature summary table

	SignalP 3.0a	TMHMM	Hit to PDB (getstruct)	IletPhos	pfam
AP000295.6-001	Signal peptide? (Y/N) 26 res. (7%)	TM helix 46 res. (13%) Outside 217 res. (65%) Inside 68 res. (20%)	Matching 210 res. (83%)	Predicted 44 res. (13%)	Interfer- 103 res. (31%) bind
AP000295.6-003	Signal peptide? (Y/N) 26 res. (10%)	TM helix 23 res. (9%) Outside 210 res. (87%) Inside 6 res. (2%)	Matching 212 res. (88%)	Predicted 29 res. (12%)	Interfer- 103 res. (43%) bind
AP000295.6-007	(no output)	TM helix 23 res. (15%) Outside 68 res. (44%) Inside 62 res. (40%)	Matching 57 res. (37%) Mismatch(gap) 1 res. (0%)	Predicted 21 res. (13%)	Interfer- 61 res. (39%) bind
AP000295.6-008	Signal peptide? (Y/N) 26 res. (14%)	TM helix 23 res. (12%) Outside 151 res. (83%) Inside 6 res. (3%)	Matching 153 res. (85%)	Predicted 23 res. (12%)	Interfer- 44 res. (24%) bind

2D feature alignment plot

3D structural annotation plot

Isoform 1

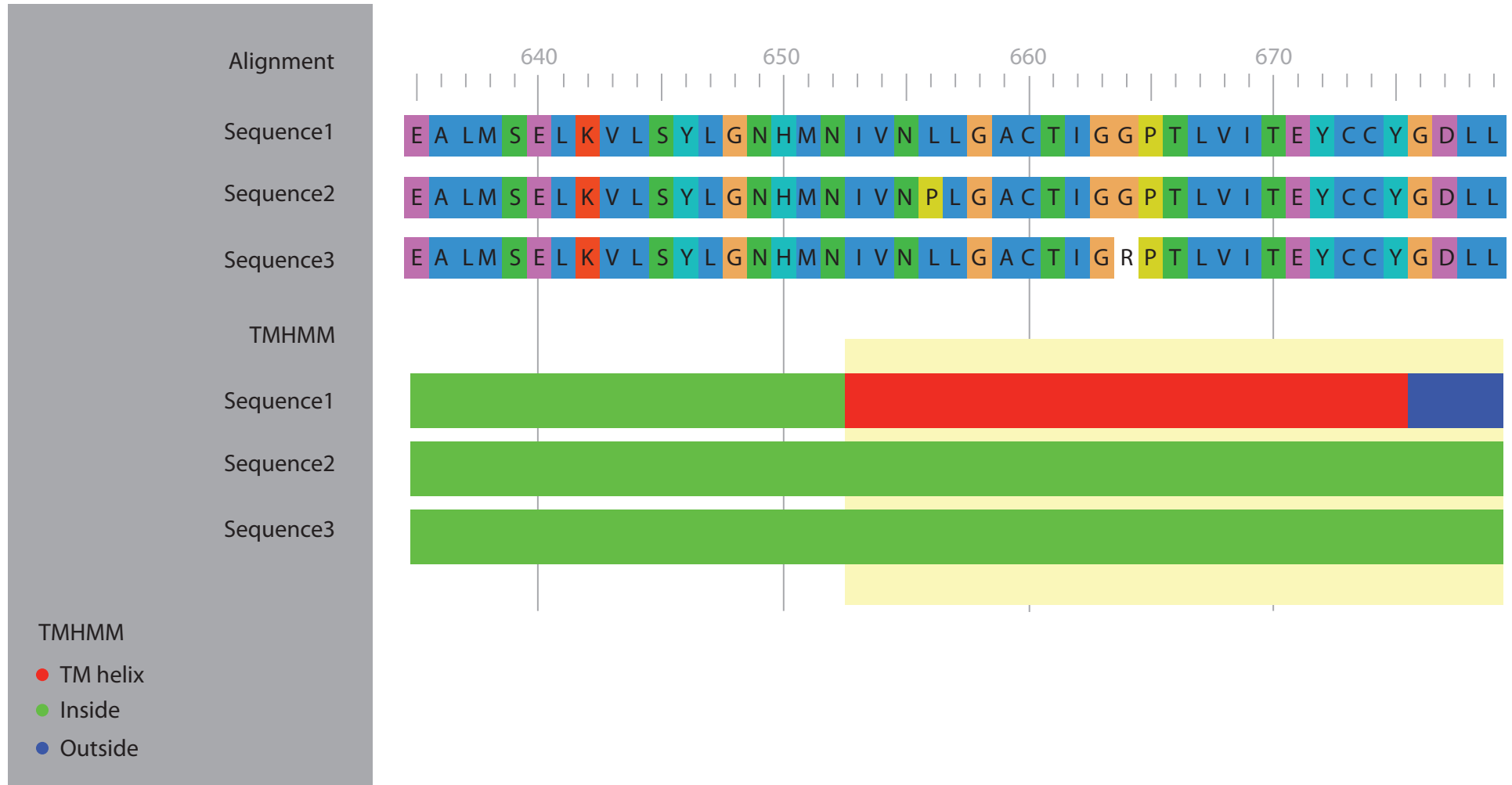
Isoform 2

Isoform 3

Isoform 4

The workflow in the Epipe method [8] which is designed to identify functional differences between sequence variants as they are produced by alternative splicing, SNPs, or somatic mutations. The isoforms are first aligned, then analyzed by a large number of feature predictors, and finally differential features are extracted and presented and mapped onto protein structural information if available in PDB.

Sequence1	Reference KIT_HUMAN	976 res.
Sequence2	L656P KIT_HUMAN	976 res.
Sequence3	G664R KIT_HUMAN	976 res.



An example output from Epipe for variants of the receptor for stem-cell growth factor (mast-cell growth factor) KIT_Human, which has tyrosine protein kinase activity. Binding of ligands leads to the autophosphorylation of KIT and its association with substrates such as phosphatidylinositol 3-kinase (PI3K). The prediction shows that several single amino-acid changes can lead to a complete shift in the prediction of the membrane protein topology using the TMHMM method [36].