CONSERVATION OF FUNCTIONAL REGIONS IN THE STARD11 LIPID TRANSFER DOMAIN

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INTRODUCTION AND OBJECTIVES

STARD11 is a protein domain that transfers ceramide from the ER membrane to the Golgi membrane. It belongs to the superfamily of StAR-related lipid-transfer domains (STARD) which contains 13 other members. Other STARD proteins transfer different types of lipids.[1]

The main aim of this study was to investigate the START-domain of the human STARD11. Questions to be answered:

1. **Is the membrane-binding region conserved?** Investigated STARD11 in other organisms as well as human STARD proteins.
2. **Is the ceramide-binding region conserved**? Investigated STARD11 in other organisms as well as human STARD proteins.
3. **Is the membrane binding region flexible?** Investigated STARD11 in WebNma and presenting a fluctuation diagram.

MATERIALS AND METHODS

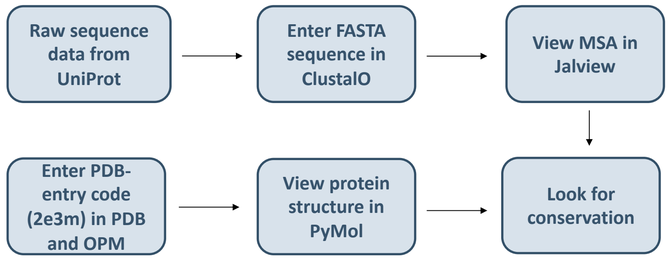

Figure 1: Flow chart of the bioinformatic strategy used in this research. Tools: UniProt, ClustalO[2], Jalview[3], **P**rotein **D**ata **B**ank, PyMol, OPM[4], WebNma[5] and WebLogo[5].

RESULTS OVERVIEW

A

	STARD9	STARD1	STARD3	STARD4	STARD5	STARD6	STARD8	STARD13	STARD11	STARD10	STARD2	STARD 7
STARD9	100,00	17,00	16,00	9,00	19,00	12,00	15,00	15,00	18,00	15,00	13,00	13,00
STARD1	17,00	100,00	36,00	16,00	23,00	22,00	16,00	20,00	14,00	17,00	14,00	15,00
STARD3	16,00	23,00	100,00	21,00	23,00	20,00	21,00	14,00	16,00	16,00	12,00	15,00
STARD4	10,00	16,00	21,00	100,00	32,00	20,00	14,00	13,00	15,00	15,00	11,00	14,00
STARD5	19,00	22,00	24,00	32,00	100,00	33,00	19,00	19,00	17,00	20,00	15,00	17,00
STARD6	13,00	22,00	20,00	28,00	33,00	100,00	15,00	15,00	13,00	15,00	15,00	15,00
STARD8	15,00	15,00	14,00	16,00	18,00	15,00	100,00	56,00	16,00	16,00	14,00	18,00
STARD13	14,00	20,00	13,00	15,00	18,00	15,00	56,00	100,00	18,00	18,00	12,00	18,00
STARD11	18,00	14,00	15,00	16,00	17,00	13,00	16,00	18,00	100,00	20,00	20,00	16,00
STARD10	15,00	17,00	15,00	16,00	20,00	15,00	16,00	18,00	20,00	100,00	24,00	21,00
STARD2	13,00	14,00	11,00	17,00	15,00	25,00	14,00	12,00	20,00	24,00	100,00	25,00
STARD 7	12,00	15,00	14,00	18,00	17,00	15,00	18,00	18,00	16,00	21,00	25,00	100,00

B

	ringworm	zebrafish	chimpanzee	human	whale	elephant	mouse	fruit flies	bug
ringworm	100	29	30	36	30	29	31	35	34
zebrafish	29	100	87	86	86	79	86	43	51
chimpanzee	30	87	100	98	87	92	96	39	52
human	36	86	98	100	96	97	96	44	50
whale	30	86	87	96	100	92	96	38	52
elephant	29	79	92	97	92	100	90	38	49
mouse	31	86	96	96	96	90	100	38	50
fruit flies	35	43	39	44	38	38	38	100	49
bug	34	51	52	50	52	49	50	49	100

Figure 2: Heat map based on a percentage identity matrix obtained from ClustalO of different human STARD proteins (A) and different species of STARD11 (B). This heatmap illustrates which proteins have low sequence similarity (red) and which proteins have high sequence similarity (green).

RESULTS QUESTION 1 AND 2

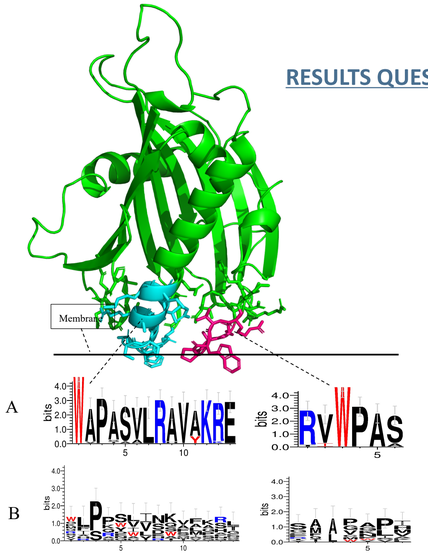

Figure 3: Comparison of the membrane binding site in various STARD11 species (A) and STARD proteins (B). The membrane binding site is more conserved in the different species compared to different human STARD proteins.

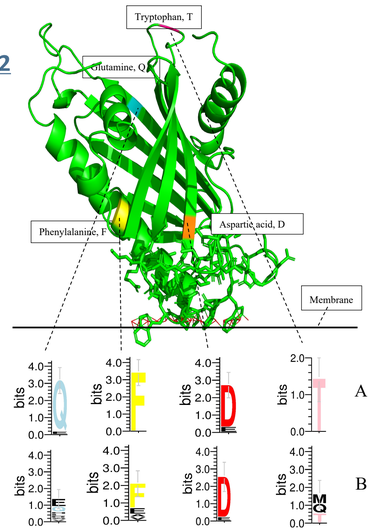

Figure 4: Comparison of the Ceramide binding site in various STARD11 species (A) and STARD proteins (B). The ligand binding site is more conserved in the different species compared to different human STARD proteins.

RESULTS QUESTION 3

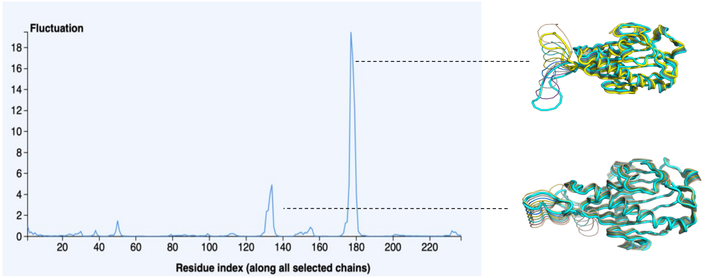

Figure 5: Flexibility profile of the STARD11 domain and PyMol representation of the two most flexible nodes. Ligand binding site 479 (D) and 579 (F) is present in node 1 and 2, respectively. These two nodes are located at the opposite site of the membrane binding region.

CONCLUSION

- **Overview**: Other organisms that contain STARD11 have conserved both the membrane and the ceramide binding site, but not other human STARD proteins.
- **Q1**: The amino acid W is highly conserved in the membrane binding site between the different species[1].
- **Q2**: The ligand binding site 479 (D) and 579 (F) are conserved in both other organisms with STARD11 and other human STARD proteins.
- **Q3**: Two ligand binding sites are found in the two flexible regions, node 1 and 2. This could explain how STARD11 attracts ceramides and shelters them.

FURTHER STUDIES

- Investigate why the most flexible regions are located at the opposite site of the membrane binding region.

REFERENCES

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