

Mapping anti-West Nile virus regions in the type I interferon-induced

Schlafen proteins

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Background

- Several members of SLFN protein family shown to have anti-viral activity
 - N-terminus of hSLFN11 and mSLFN9 impair WNV replication
- Mouse ortholog of hSLFN11 is unknown, but could help identify region of hSLFN11 N-terminus that is active against WNV replication

Question

Where is the anti-WNV active region in the SLFN proteins?

Hypothesis

mSLFN9 and mSLFN8 could be the mouse ortholog of hSLFN11 and help determine the location of the anti-WNV active region in hSLFN11

References

Valdez, F., Salvador, J., Palermo, P., Mohl, J. E., Hanley, K. A., Watts, D., & Llano, M. (2018). Schlafen 11 Restricts Flavivirus Replication. *Journal of Virology*. doi:10.1101/434563

Data

Table 1. Amino acid percent conservation between various SLFN proteins is shown. The highlighted values indicate the percentage similarity of mSLFN8 V1, mSLFN8 V2, and mSLFN9 with hSLFN11 respectively.

Percent Identity Matrix (Protein Sequence)							
	mSlfn5	mSlfn8V1	mSlfn8V2	mSlfn9	mSlfn10	hSlfn11	mSlfn14
mSlfn5	100						
mSlfn8V1	41.73	100					
mSlfn8V2	30.69	98.03	100				
mSlfn9	41.85	82.8	85.82	100			
mSlfn10	42.68	87.5	85.71	87.25	100		
hSlfn11	44.84	60.59	57.32	61.94	62.06	100	
mSlfn14	38.2	39.64	39.23	40.43	40.61	43.51	100

Figure 1. Viral concentration from A172 cells expressing various SLFN proteins is shown. The A172 hSLFN11 KD cells do not inhibit WNV replication, and cells expressing mSLFN8 V2 showed the same trend indicating that mSLFN8 V2 is not active against WNV replication.

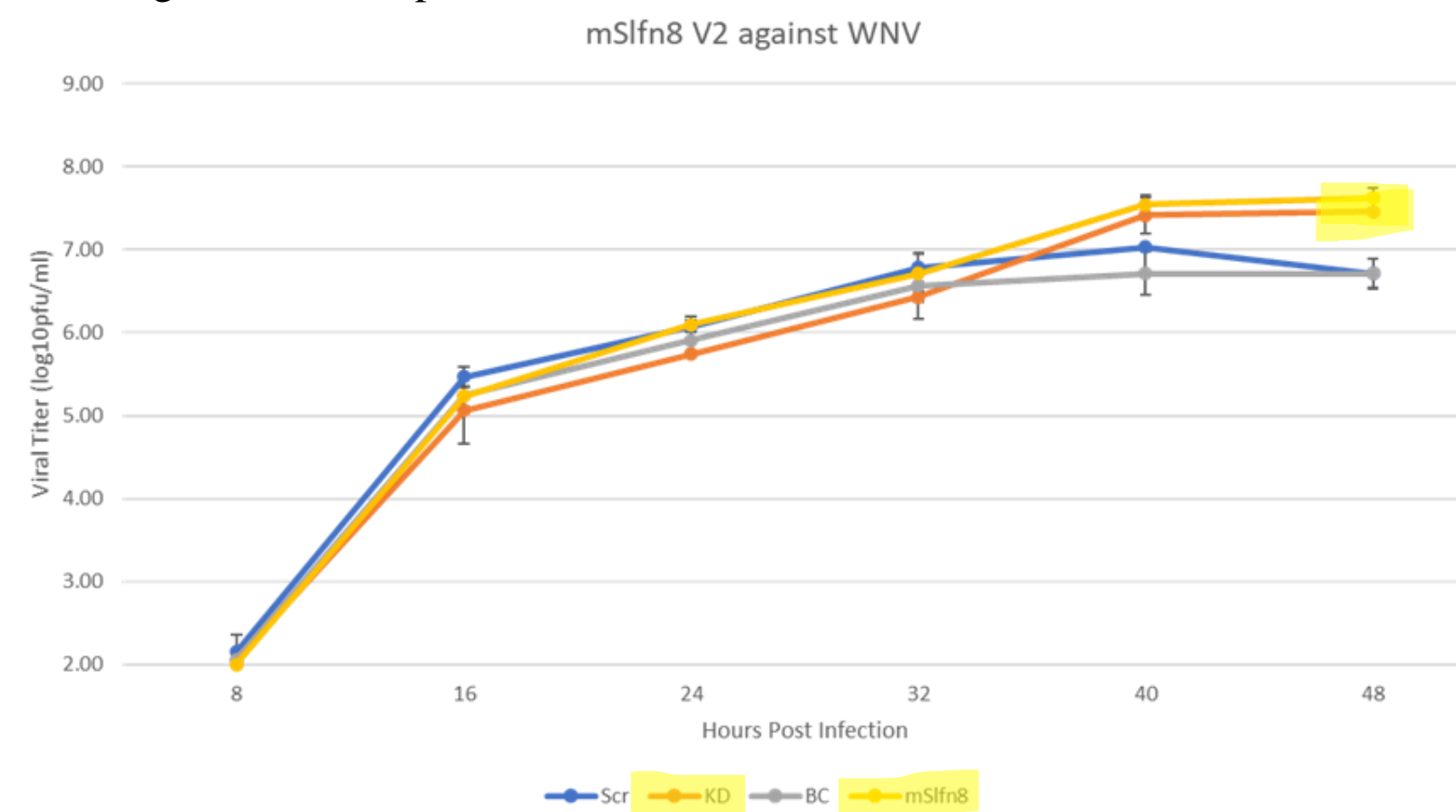


Figure 2. Protein alignment between N-terminus of hSLFN11, mSLFN8V2, and mSLFN9 is shown. The dashed line indicates that this section is missing, so the region in the red box could be the active region for anti-WNV activity.

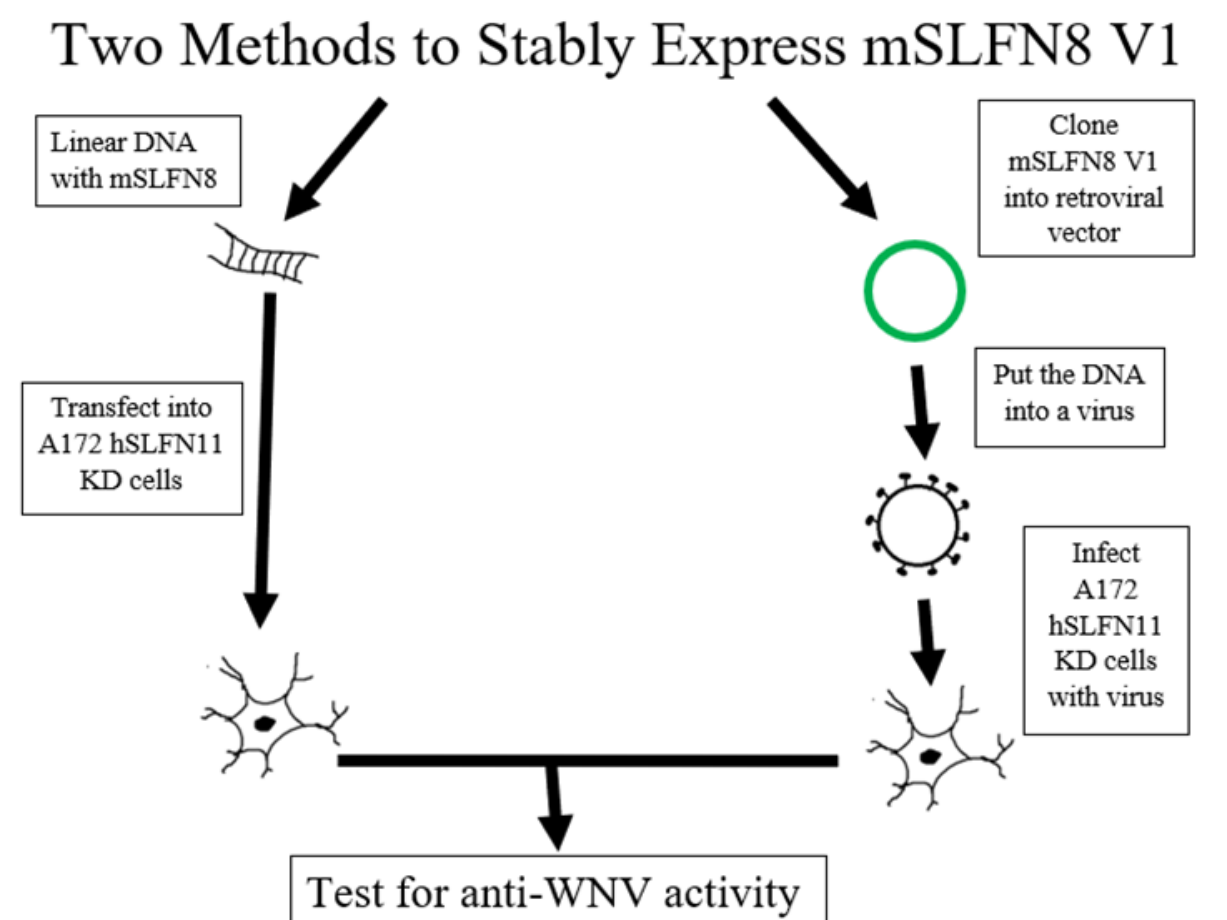
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hSlfn11-N-term  ESLWRDLISEHRGLEELINKQMQFFFRGILIF-----441
mSlfn8V2      ESLWSELCSQHERLEDLVKQIIRSFSCGLLIISRSWAVDNLNLEEKQEVICDALLIAQNSP407
mSlfn9        -----469
    
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Methods

Two Variants of mSLFN8 evaluated:

- mSLFN8 V2 stably expressed in cells, then tested for anti-WNV activity
- Two methods to stably express mSLFN8 V1 currently being conducted, then will be tested for anti-WNV activity.



Conclusion

Because mSLFN8 V2 is not active against WNV, amino acid 408-441 in mSLFN9 and hSLFN11 could be anti-WNV active region. Once mSLFN8 V1 has been tested for anti-WNV activity, a more thorough location of the active region will be established.

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