

# Significant protein sequence alignment between *Saccharomyces cerevisiae* proteins (a vaccine contaminant) and Systemic Lupus Erythematosus associated autoepitopes

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## Background

Anti-RNP antibody and anti-Sm antibody were identified as risk factors for Systemic Lupus Erythematosus (SLE) associated pulmonary arterial hypertension.<sup>1</sup>

Rinaldi et al.<sup>2</sup> describe *Saccharomyces cerevisiae* mannan related SLE autoantibodies.

Vaccine antigens can result in autoimmunity due to molecular mimicry as we have seen in the case of Pandemrix induced narcolepsy.<sup>3</sup>

Hepatitis B vaccines, HPV vaccines and some other vaccines are produced using yeast (*S. cerevisiae*)<sup>4</sup>. Since vaccines can be contaminated with any protein from *S. cerevisiae*, BLASTP comparisons were run for the entire organism (not just mannan). Results are presented below.

SLE has been associated with the Hepatitis B and other vaccines.<sup>5,6</sup>

IOM report on vaccine adverse events 2012<sup>7</sup> says:

“Poirriez (2004) reported the absorption of antinuclear antibodies (ANAs), isolated from a single hepatitis B immunized patient who developed lupus, by highly concentrated vaccine antigen suggesting mimicry between vaccine antigen and self-antigen.”

SLE has been associated with the HPV vaccine.<sup>8</sup>

SLE has been associated with the Epstein-Barr virus (EBV).<sup>9</sup>

BLASTP results for EBV are also included below.

## Method

Protein sequences for the autoantigens were obtained from Uniprot.<sup>10</sup>

[BLASTP](#) methodology used was previously described.<sup>11</sup>

## Results

### 1. Strong alignment between human U1 snRNP<sup>1,12</sup> and *S.cerevisiae*.

U1 small nuclear ribonucleoprotein 70 kDa (human) vs. *S.cerevisiae*

SnP1p [*Saccharomyces cerevisiae* YJM270]

Sequence ID: AJR37623.1Length: 300Number of Matches: 1

#### Related Information

Identical Proteins-Identical proteins to EHN06639.1

Range 1: 15 to 200GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score Expect Method Identities Positives Gaps

87.8 bits(216) 2e-18 Compositional matrix adjust. 67/195(34%) 105/195(53%) 22/195(11%)

Query 12 LFAPRDPIPYLPPLEKLPHEKHHNQPYCGIAP-----YIREFEDPRDAPPPTRAET 62

LF PR P+ Y P+ P+ K P G+A Y+ EF P +P

Sbjct 15 LFKPRPLSYKRPTD-YPYAKRQTNPNITGVANLLSTSLKHYMEEF--PEGSP-----NN 66

Query 63 REERMERKRREKIERRQQEVETELKMWDPHNDPNAQ-GDAFKTLFVARVNYDTTESKLRR 121

+R E + KI + Q ++ L+ W+P+ DP+ + D ++T+F+ R+ YD E +L++

Sbjct 67 HLQRYEDIKLSKI-KNAQLLDRRLQNWNPNVDPHIKDTDPYRTIFIGRLPYDLDEIELQK 125

Query 122 EFEVYGPIKRIHVMVYSKRSKGPRGYAFIEYEHEDMHSAYKHAD---GKKIDGRRVLVDV 178

F +G I++I+V K +K +GYAFI ++ A+K G +I GR +VD+

Sbjct 126 YFVKFGEIEKIRIVKDKITQKSKGYAFIVFKDPISSKMAFKEIGVHRGIQIKGRVCIVDI 185

Query 179 ERGRTVKGWRPRRLG 193

ERGRTVK ++PRRLG

Sbjct 186 ERGRTVKYFKPRRLG 200

## 2. Strong alignment between human Sm B/B'<sup>1,12</sup> and *S. cerevisiae*

Small nuclear ribonucleoprotein-associated proteins B and B' (human) vs. *S. cerevisiae*

Smb1p [*Saccharomyces cerevisiae* YJM1615]

Sequence ID: AJU45326.1Length: 196Number of Matches: 1

#### Related Information

Range 1: 4 to 101GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score Expect Method Identities Positives Gaps

87.8 bits(216) 2e-20 Compositional matrix adjust. 45/98(46%) 62/98(63%) 12/98(12%)

Query 1 MTVGKSSKMLQHIDYRMRCILQDGRIFIGTFKAFDKHMNLILCDCDEFR-----KIKP 53

+ V SS++ IDY++R + QDGR++IG AFDKHMNL+L +C E R K++P

Sbjct 4 IQVAHSSRLANLIDYKLRVLTQDGRVYIGQLMAFDKHMNLVLNECIEERVPKTQLDKLRP 63

Query 54 -KNSKQAE---REEKRVLGLVLLRGENLVSMTVEGPP 86

K+SK + EKRVLGL +LRGE ++S VE P

Sbjct 64 RKDSKDGTTLNKVEKRVLGLTILRGEQILSTVVEDKP 101

## 3. Strong and comparable alignment between human SNRPD1<sup>1,12</sup> vs. both *S. cerevisiae* and EBV

SNRPD1 (human) vs. *S. cerevisiae*

Snf2p [*Saccharomyces cerevisiae* YJM1386]

Sequence ID: AJU00532.1Length: 1708Number of Matches: 10

#### Related Information

Range 1: 1509 to 1527GenPeptGraphicsNext MatchPrevious Match  
Alignment statistics for match #1  
Score Expect Identities Positives Gaps  
59.2 bits(132) 2e-11 19/19(100%) 19/19(100%) 0/19(0%)  
Query 3 GRGRGRGRGRGRGRGRGRG 21  
GRGRGRGRGRGRGRGRGRG  
Sbjct 1509 GRGRGRGRGRGRGRGRGRG 1527

SNRPD1 (human) vs. Epstein-Barr virus (EBV)

EBNA-1 [Cynomolgus Epstein-Barr Virus Si-IIA]  
Sequence ID: BAB03282.1Length: 588Number of Matches: 11  
Related Information  
Range 1: 267 to 293GenPeptGraphicsNext MatchPrevious Match  
Alignment statistics for match #1  
Score Expect Identities Positives Gaps  
58.7 bits(131) 3e-11 22/27(81%) 22/27(81%) 5/27(18%)  
Query 3 GRGRGRG--RGRGRGRGRGRG---GPR 24  
GRGRGRG RGRGRGRGRGRG GPR  
Sbjct 267 GRGRGRGGSRGRGRGRGRGRGRGQGPR 293

#### 4. Significant and comparable alignment between human SNRPD1<sup>1,12</sup> vs. both Hepatitis B virus and HPV

Note: Hepatitis B and HPV vaccines are manufactured using recombinant technology to produce virus like particles (VLP).<sup>13-15</sup> The BLAST database only contains the whole virus entries, not VLPs.

Therefore, the Hepatitis B core protein result below may only apply to Hepatitis B infections and not to Hepatitis B immunization with recombinant vaccines.

SNRPD1 (human) vs. Hepatitis B virus

core protein [Hepatitis B virus]  
Sequence ID: ANQ90213.1Length: 185Number of Matches: 2  
Related Information  
Range 1: 150 to 160GenPeptGraphicsNext MatchPrevious Match  
Alignment statistics for match #1  
Score Expect Identities Positives Gaps  
29.5 bits(62) 0.017 10/12(83%) 10/12(83%) 1/12(8%)  
Query 14 RGRGRGRGGPRR 25  
RGRGRGR PRR  
Sbjct 150 RGRGRGR-SPRR 160

SNRPD1 (human) vs. HPV virus

E2 [Human papillomavirus]  
Sequence ID: AQM73700.1Length: 433Number of Matches: 1  
Related Information  
Range 1: 289 to 310GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score Expect Identities Positives Gaps  
27.4 bits(57) 0.097 14/24(58%) 14/24(58%) 5/24(20%)  
Query 4 RGRGRGRGRGRG---RGRGRGGPR 24  
RG GR RG GRG R R R G R  
Sbjct 289 RG-GR-RGSGRGPLTRSRSRSGSR 310

5. Significant and comparable alignment between Human Sm B/B'<sup>1,9,12</sup> target vs. both *S. cerevisiae* and EBV.

PPPGMRPP<sup>9,16</sup> vs. *S. cerevisiae*

chromosome stability-related protein [Saccharomyces cerevisiae YJM789]

Sequence ID: EDN59297.1Length: 482Number of Matches: 1

See 32 more title(s)

Related Information

Identical Proteins-Identical proteins to EDN59297.1

Range 1: 280 to 286GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score Expect Identities Positives Gaps  
21.4 bits(43) 23 6/7(86%) 6/7(85%) 0/7(0%)

Query 1 PPPGMRP 7

PPPGM P

Sbjct 280 PPPGMNP 286

PPPGMRPP<sup>9,16</sup> vs EBV

EBNA1 [Human gammaherpesvirus 4]

Sequence ID: ALV83108.1Length: 685Number of Matches: 1

Related Information

Range 1: 442 to 448GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score Expect Identities Positives Gaps  
21.0 bits(42) 33 6/7(86%) 6/7(85%) 0/7(0%)

Query 1 PPPGMRP 7

PPPG RP

Sbjct 442 PPPGRRP 448

6. Significant alignment between the peptide sequence leading to Ro autoimmunity in SLE (TKYKQRNGWSHK)<sup>9</sup> and *S. cerevisiae*.

TKYKQRNGWSHK<sup>9</sup> vs. *S. cerevisiae*

Bag7p [Saccharomyces cerevisiae YJM1388]

Sequence ID: AJU01372.1Length: 404Number of Matches: 1

See 2 more title(s)

Related Information

Identical Proteins-Identical proteins to AJU01372.1

Range 1: 384 to 392GenPeptGraphicsNext MatchPrevious Match

Alignment statistics for match #1

Score	Expect	Identities	Positives	Gaps
21.0 bits(42)	76	6/9(67%)	6/9(66%)	0/9(0%)
Query 1	TKYKQRNGW	9		
	TK KQR	W		
Sbjct 384	TKHKQRQSW	392		

#### 7. Significant alignment between the cross-reactive epitope of EBNA-1 (GGSGSGPRHRDGVRR)<sup>9</sup> and *S. cerevisiae*.

GGSGSGPRHRDGVRR<sup>9</sup> vs. *S. cerevisiae*

Rfm1p [Saccharomyces cerevisiae YJM1463]  
Sequence ID: AJU10280.1Length: 310Number of Matches: 1  
Related Information  
Range 1: 191 to 196GenPeptGraphicsNext MatchPrevious Match  
Alignment statistics for match #1  
Score Expect Identities Positives Gaps  
20.2 bits(40) 252 5/6(83%) 6/6(100%) 0/6(0%)  
Query 10 RDGVRR 15  
RDG+RR  
Sbjct 191 RDGIRR 196

## Conclusion

*Saccharomyces cerevisiae* (yeast) contaminated vaccines such as Hepatitis B and HPV vaccines can cause the synthesis of SLE associated autoantibodies. *S. cerevisiae* and Epstein-Barr virus are comparable in molecular mimicry of multiple self antigens. So they seem equally capable of causing SLE autoimmunity.

## Action

All contaminating proteins in vaccines must be removed immediately.<sup>17</sup> All proteins in vaccines needed for disease protection must also be thoroughly scrutinized for molecular mimicry that can result in allergic or autoimmune diseases.

## References

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