

**Title:** Identification of the *Streptococcus pyogenes* surface antigens recognised by pooled human immunoglobulin

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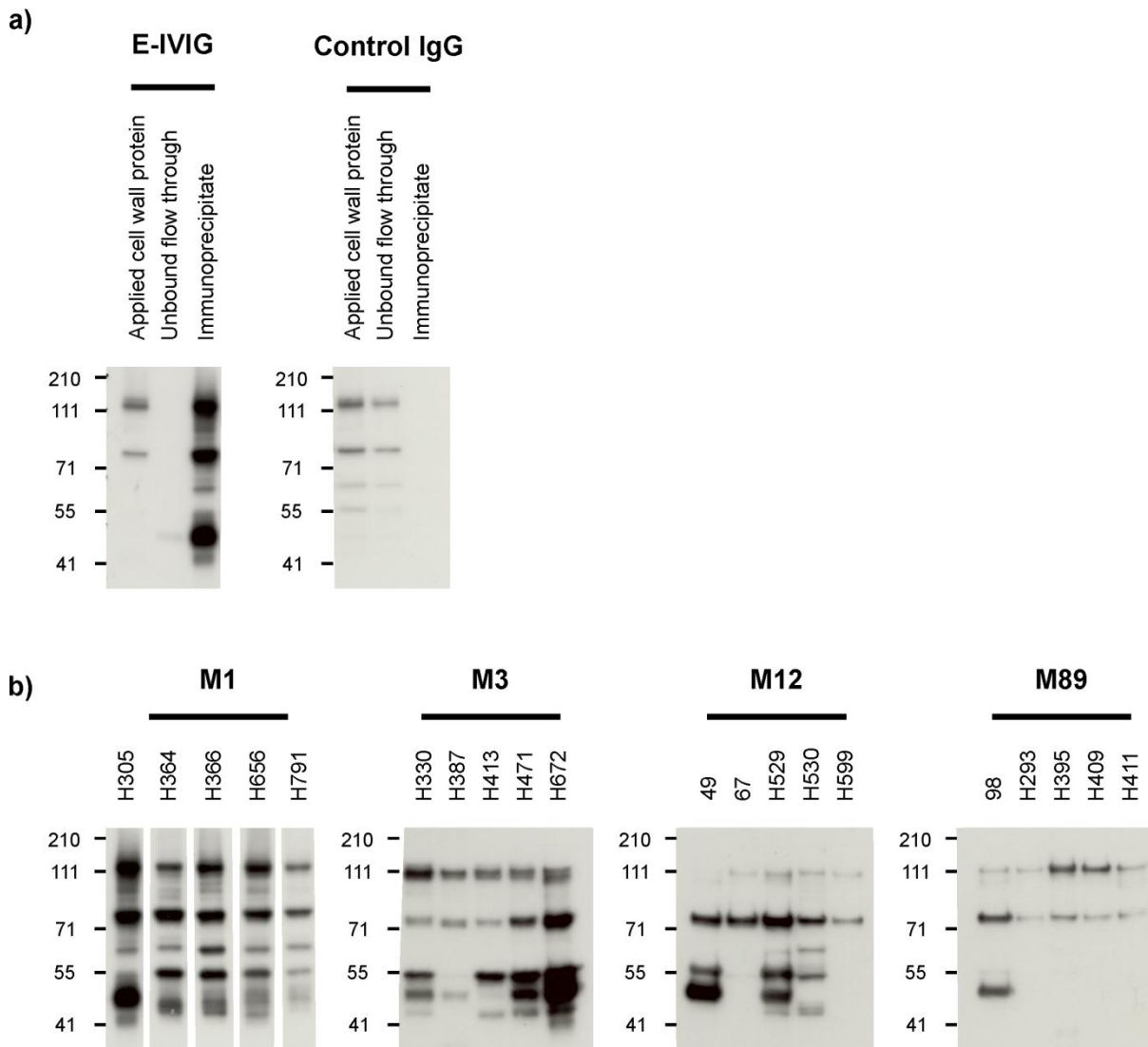
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## Supporting information



**Supplementary Figure 1: Purification of *S. pyogenes* surface antigens by E-IVIG immunoprecipitation.** A) In preliminary experiments antigenic proteins were purified from serotype M1 cell wall extract (strain H305) by immunoprecipitation using E-IVIG or polyclonal goat (control) IgG. Aliquots of the applied cell wall extract, the column flow through and the resulting immunoprecipitate were separated on 7% tris-acetate gels and subjected to immunoblot analysis using IVIG as the primary antibody. B) The immunoprecipitates recovered from the 20 strains selected for study were separated on 7% TA gels and subjected to immunoblot analysis using IVIG as the primary antibody. Molecular mass markers are given in kilodaltons.

**Supplementary Table 1: *S. pyogenes* isolates used in this study**

<b>M type/Isolate</b>	<b>Source</b>	<b>Disease manifestation</b>
<b>M1</b>		
H305	Throat	Scarlet fever
H364*	Lung	Pneumonia/septic shock
H366*	Blood	Pneumonia/septic shock
H656	Blood	Bacteremia
H791	Blood	Cellulitis
<b>M3</b>		
H330*	Blood	Puerperal sepsis
H387	Throat	Septic shock
H413	-	Septic shock
H471*	Ear	Septic shock
H672	Throat	Tonsillitis
<b>M12</b>		
49	Throat	Tonsillitis
67	Throat	Tonsillitis
H529	Blood	Septic shock
H530*	Blood	Septic shock
H599*	Blood	Bacteremia
<b>M89</b>		
98 <sup>†</sup>	Throat	Tonsillitis
H293*	Muscle	Necrotizing fasciitis/septic shock
H395 <sup>‡</sup>	Blood	Pneumonia
H409	Invasive	Septic shock
H411	Blood	Bacteremia

\*Isolates used in opsonophagocytic uptake assays

<sup>†</sup>Genetically acapsular <sup>16</sup>

<sup>‡</sup>Hyperencapsulated *covS* mutant <sup>16</sup>

**Supplementary Table 2: The *S. pyogenes* antigens purified by E-IVIG immunoprecipitation.** Numbers represent the proportion of strains from which targets were identified.

Uniprot identifier	Gene	Protein product	SEQUEST P-values (range)	M1	M3	M12	M89	Total	
C5AP_STRP1	<i>scpA</i> , SPy_2010, M5005_Spy1715	C5a peptidase	1x10 <sup>-30</sup> - 7x10 <sup>-10</sup>	5/5	5/5	5/5	5/5	20/20	100%
DNAK_STRP1	<i>dnaK</i> , SPy_1760, M5005_Spy1498	Chaperone protein DnaK	8x10 <sup>-15</sup> - 8x10 <sup>-8</sup>	5/5	5/5	5/5	5/5	20/20	
Q48Y96_STRP1	<i>malE</i> , M5005_Spy1058, SPy_1294	Maltose/maltodextrin-binding protein	2x10 <sup>-16</sup> - 3x10 <sup>-10</sup>	5/5	5/5	5/5	5/5	20/20	
Q490V0_STRP1	<i>oppA</i> , M5005_Spy0249	Oligopeptide-binding protein	1x10 <sup>-30</sup> - 2x10 <sup>-10</sup>	5/5	5/5	5/5	5/5	20/20	
Q491G2_STRP1	M5005_Spy0137	Nucleoside-binding protein	1x10 <sup>-30</sup> - 1x10 <sup>-15</sup>	5/5	5/5	5/5	5/5	20/20	
Q99XX8_STRP1	<i>pulA</i> , SPy_1972	Putative pullulanase	2x10 <sup>-14</sup> - 6x10 <sup>-8</sup>	5/5	5/5	5/5	5/5	20/20	
Q99ZH4_STRP1	M5005_Spy0942, SPy_1228	Nucleoside-binding protein	1x10 <sup>-30</sup> - 7x10 <sup>-11</sup>	5/5	5/5	5/5	5/5	20/20	
Q99ZW9_STRP1	M5005_Spy0762, SPy_1037	Hypothetical membrane associated protein	1x10 <sup>-30</sup> - 2x10 <sup>-13</sup>	5/5	5/5	5/5	5/5	20/20	
Q9A0C0_STRP1	M5005_Spy0651, SPy_0843	Cell surface protein	7x10 <sup>-14</sup> - 3x10 <sup>-7</sup>	5/5	5/5	5/5	5/5	20/20	
Q9A1H3_STRP1	<i>prgA</i> , M5005_Spy0229, SPy_0269	SpyAD	2x10 <sup>-15</sup> - 4x10 <sup>-11</sup>	5/5	5/5	5/5	5/5	20/20	
EFTS_STRP1	<i>tsf</i> , SPy_2093, M5005_Spy1781	Elongation factor Ts	3x10 <sup>-15</sup> - 3x10 <sup>-8</sup>	5/5	5/5	4/5	5/5	19/20	70-95%
MTSA_STRP1	<i>mtsA</i> , SPy_0453, M5005_Spy0368	Metal ABC transporter substrate-binding lipoprotein	1x10 <sup>-30</sup> - 9x10 <sup>-10</sup>	5/5	5/5	4/5	5/5	19/20	
PGK_STRP1	<i>pgk</i> , SPy_1881, M5005_Spy1599	Phosphoglycerate kinase	6x10 <sup>-14</sup> - 5x10 <sup>-9</sup>	5/5	3/5	5/5	5/5	18/20	
Q99YL6_STRP1	SPy_1643	Putative uncharacterized protein	2x10 <sup>-9</sup> - 2x10 <sup>-6</sup>	4/5	4/5	5/5	5/5	18/20	
Q9A0C5_STRP1	SPy_0836	Putative uncharacterized protein	1x10 <sup>-10</sup> - 6x10 <sup>-5</sup>	5/5	3/5	5/5	5/5	18/20	
TACY_STRP1	<i>slo</i> , SPy_0167, M5005_Spy0141	Streptolysin O	1x10 <sup>-30</sup> - 5x10 <sup>-7</sup>	5/5	5/5	5/5	3/5	18/20	
PEPDB_STRP1	<i>pepDB</i> , SPy_2066, M5005_Spy1758	Probable dipeptidase B	1x10 <sup>-30</sup> - 2x10 <sup>-7</sup>	4/5	3/5	5/5	5/5	17/20	
Q7DAN2_STRP1	<i>nga</i> , SPy_0165	Nicotine adenine dinucleotide glycohydrolase	8x10 <sup>-15</sup> - 3x10 <sup>-11</sup>	5/5	5/5	5/5	2/5	17/20	
Q9A1G0_STRP1	<i>dacA</i> , <i>dacA2</i> , M5005_Spy0248, SPy_0292	Penicillin-binding protein (D-alanyl-D-alanine carboxypeptidase)	9x10 <sup>-12</sup> - 1x10 <sup>-4</sup>	2/5	5/5	5/5	5/5	17/20	
Q490K8_STRP1	M5005_Spy0341	SpyCEP	3x10 <sup>-15</sup> - 1x10 <sup>-5</sup>	5/5	5/5	2/5	4/5	16/20	
Q99XU2_STRP1	M5005_Spy1728, SPy_2032	Periplasmic component of efflux system	3x10 <sup>-13</sup> - 9x10 <sup>-9</sup>	5/5	3/5	3/5	5/5	16/20	
Q48XJ9_STRP1	M5005_Spy1308, SPy_1592	Sugar-binding protein	3x10 <sup>-15</sup> - 2x10 <sup>-5</sup>	5/5	3/5	1/5	5/5	14/20	
Q99XV0_STRP1	<i>emm1</i> , SPy_2018	M protein type 1	5x10 <sup>-13</sup> - 5x10 <sup>-6</sup>	5/5	5/5	4/5	0/5	14/20	
EFG_STRP1	<i>fus</i> , SPy_0273, M5005_Spy0232	Elongation factor G	6x10 <sup>-16</sup> - 8x10 <sup>-5</sup>	5/5	2/5	2/5	4/5	13/20	50-65%
Q9A147_STRP1	M5005_Spy0384, SPy_0469	Putative 42 kDa protein	7x10 <sup>-10</sup> - 7x10 <sup>-4</sup>	5/5	1/5	4/5	3/5	13/20	
PURA_STRP1	<i>purA</i> , SPy_0160, M5005_Spy0136	Adenylosuccinate synthetase	2x10 <sup>-13</sup> - 3x10 <sup>-5</sup>	5/5	2/5	2/5	3/5	12/20	
Q48Y78_STRP1	<i>glnH</i> , M5005_Spy1076	Transporter	1x10 <sup>-30</sup> - 4x10 <sup>-6</sup>	3/5	2/5	5/5	2/5	12/20	
Q99ZT1_STRP1	M5005_Spy0818, SPy_1094	Polysaccharide deacetylase	8x10 <sup>-10</sup> - 8x10 <sup>-7</sup>	3/5	0/5	5/5	4/5	12/20	
PILIN_STRP1	SPy_0128, M5005_Spy0109	Pilin	1x10 <sup>-15</sup> - 1x10 <sup>-13</sup>	5/5	5/5	1/5	0/5	11/20	
Q48ZH8_STRP1	M5005_Spy0622	Phosphoglycerol transferase	3x10 <sup>-13</sup> - 3x10 <sup>-5</sup>	5/5	1/5	1/5	4/5	11/20	
Q491J2_STRP1	M5005_Spy0107	Fibronectin-binding protein	1x10 <sup>-30</sup> - 6x10 <sup>-7</sup>	5/5	5/5	1/5	0/5	11/20	
Q99YQ4_STRP1	SPy_1591	Putative uncharacterized protein	2x10 <sup>-11</sup> - 2x10 <sup>-4</sup>	4/5	1/5	1/5	5/5	11/20	
Q99Z76_STRP1	<i>inlA</i> , M5005_Spy1109, SPy_1361	Internalin protein	1x10 <sup>-11</sup> - 1x10 <sup>-6</sup>	4/5	4/5	2/5	1/5	11/20	
SPEB_STRP1	<i>speB</i> , SPy_2039, M5005_Spy1735	Streptopain	4x10 <sup>-15</sup> - 1x10 <sup>-6</sup>	5/5	1/5	1/5	4/5	11/20	
Q99ZX4_STRP1	<i>hylA</i> , M5005_Spy0757, SPy_1032	Extracellular hyaluronate lyase	2x10 <sup>-15</sup> - 7x10 <sup>-4</sup>	5/5	0/5	3/5	2/5	10/20	
Q9A0J7_STRP1	M5005_Spy0571, SPy_0747	Endonuclease/exonuclease/phosphatase family protein	6x10 <sup>-14</sup> - 1x10 <sup>-6</sup>	5/5	1/5	2/5	2/5	10/20	

**Supplementary Table 2 continued:**

Uniprot identifier	Gene	Protein product	SEQUEST P-values (range)	M1	M3	M12	M89	Total	
ENO_STRP1	<i>eno</i> , <i>SPy_0731</i> , <i>M5005_Spy0556</i>	Enolase	1x10 <sup>-30</sup> - 5x10 <sup>-9</sup>	4/5	1/5	2/5	2/5	9/20	
G3P_STRP1	<i>gap</i> , <i>gapA</i> , <i>plr</i> , <i>SPy_0274</i> , <i>M5005_Spy0233</i>	Glyceraldehyde-3-phosphate dehydrogenase	1x10 <sup>-30</sup> - 1x10 <sup>-6</sup>	5/5	1/5	1/5	2/5	9/20	
Q491G0_STRP1	<i>nga</i> , <i>M5005_Spy0139</i>	NAD glycohydrolase	6x10 <sup>-13</sup> - 2x10 <sup>-7</sup>	4/5	3/5	2/5	0/5	9/20	
Q99ZB1_STRP1	<i>malX</i> , <i>M5005_Spy1067</i> , <i>SPy_1306</i>	Maltose/maltodextrin-binding protein	6x10 <sup>-15</sup> - 5x10 <sup>-9</sup>	5/5	0/5	0/5	4/5	9/20	
CH60_STRP1	<i>groL</i> , <i>groEL</i> , <i>SPy_2070</i> , <i>M5005_Spy1761</i>	60 kDa chaperonin	6x10 <sup>-13</sup> - 1x10 <sup>-7</sup>	5/5	1/5	2/5	0/5	8/20	
Q9A1U2_STRP1	<i>pbp1b</i> , <i>M5005_Spy0082</i> , <i>SPy_0097</i>	Multimodular transpeptidase-transglycosylase PBP 1B	2x10 <sup>-9</sup> - 1x10 <sup>-5</sup>	5/5	0/5	1/5	2/5	8/20	
Q9A209_STRP1	<i>dnaI</i> , <i>M5005_Spy0002</i> , <i>SPy_0003</i>	DNA polymerase III subunit beta	4x10 <sup>-9</sup> - 3x10 <sup>-7</sup>	5/5	0/5	3/5	0/5	8/20	
Q99XV4_STRP1	<i>M5005_Spy1710</i> , <i>SPy_2006</i>	Streptococcal histidine triad protein	7x10 <sup>-13</sup> - 3x10 <sup>-8</sup>	5/5	0/5	1/5	1/5	7/20	
Q9A1S0_STRP1	<i>M5005_Spy0111</i> , <i>SPy_0130</i>	Putative uncharacterized protein	6x10 <sup>-13</sup> - 8x10 <sup>-5</sup>	5/5	2/5	0/5	0/5	7/20	
STRP_STRP1	<i>ska</i> , <i>SPy_1979</i> , <i>M5005_Spy1684</i>	Streptokinase A	1x10 <sup>-30</sup> - 1x10 <sup>-4</sup>	4/5	2/5	1/5	0/5	7/20	
Q99Y99_STRP1	<i>isp2</i> , <i>M5005_Spy1531</i> , <i>SPy_1801</i>	Immunogenic secreted protein	3x10 <sup>-10</sup> - 1x10 <sup>-5</sup>	4/5	2/5	0/5	0/5	6/20	25-45%
Q99ZD1_STRP1	<i>pyk</i> , <i>M5005_Spy0988</i> , <i>SPy_1282</i>	Pyruvate kinase	2x10 <sup>-11</sup> - 1x10 <sup>-5</sup>	4/5	0/5	1/5	1/5	6/20	
Q9A180_STRP1	<i>prtS</i> , <i>SPy_0416</i>	Putative cell envelope proteinase	7x10 <sup>-5</sup> - 8x10 <sup>-4</sup>	1/5	3/5	0/5	2/5	6/20	
Q9A1I9_STRP1	<i>M5005_Spy0213</i> , <i>SPy_0252</i>	N-acetylneuraminate-binding protein	5x10 <sup>-12</sup> - 9x10 <sup>-10</sup>	5/5	0/5	0/5	1/5	6/20	
Q9A1Z8_STRP1	<i>sibA</i> , <i>M5005_Spy0017</i> , <i>SPy_0019</i>	Putative secreted protein	2x10 <sup>-13</sup> - 7x10 <sup>-8</sup>	5/5	0/5	1/5	0/5	6/20	
ADCA_STRP1	<i>adcA</i> , <i>SPy_0714</i> , <i>M5005_Spy0543</i>	Zinc-binding protein AdcA	7x10 <sup>-12</sup> - 8x10 <sup>-7</sup>	4/5	0/5	1/5	0/5	5/20	
K6PF_STRP1	<i>pfkA</i> , <i>pfk</i> , <i>SPy_1283</i> , <i>M5005_Spy0989</i>	6-phosphofructokinase	1x10 <sup>-30</sup> - 2x10 <sup>-4</sup>	4/5	0/5	1/5	0/5	5/20	
Q48WW7_STRP1	<i>endoS</i> , <i>M5005_Spy1540</i>	Endo-beta-N-acetylglucosaminidase F2	1x10 <sup>-15</sup> - 6x10 <sup>-7</sup>	1/5	0/5	1/5	3/5	5/20	
Q99XQ6_STRP1	<i>pepO</i> , <i>SPy_2095</i>	Putative endopeptidase O	2x10 <sup>-13</sup> - 6x10 <sup>-5</sup>	3/5	2/5	0/5	0/5	5/20	
Q99YF1_STRP1	<i>lytR</i> , <i>M5005_Spy1474</i> , <i>SPy_1733</i>	Putative transcription regulator	6x10 <sup>-14</sup> - 3x10 <sup>-9</sup>	5/5	0/5	0/5	0/5	5/20	
TIG_STRP1	<i>tig</i> , <i>ropA</i> , <i>SPy_1896</i> , <i>M5005_Spy1612</i>	Trigger factor	7x10 <sup>-8</sup> - 6x10 <sup>-5</sup>	5/5	0/5	0/5	0/5	5/20	

**Supplementary Table 2 continued:**

Uniprot identifier	Gene	Protein product	SEQUEST P-values (range)	M1	M3	M12	M89	Total	
ALF_STRP1	<i>fta</i> , SPy_1889, M5005_Spy1607	Fructose-bisphosphate aldolase	3x10 <sup>-13</sup> - 2x10 <sup>-5</sup>	0/5	3/5	0/5	1/5	4/20	
IMDH_STRP1	<i>guaB</i> , SPy_2206, M5005_Spy1857	Inosine-5'-monophosphate dehydrogenase	2x10 <sup>-12</sup> - 3x10 <sup>-7</sup>	4/5	0/5	0/5	0/5	4/20	
Q48YY7_STRP1	<i>dacA1</i> , M5005_Spy0817	D-alanyl-D-alanine carboxypeptidase	4x10 <sup>-12</sup> - 4x10 <sup>-8</sup>	4/5	0/5	0/5	0/5	4/20	
Q99XZ6_STRP1	M5005_Spy1659, SPy_1945	Putative uncharacterized protein	3x10 <sup>-11</sup> - 4x10 <sup>-8</sup>	1/5	2/5	1/5	0/5	4/20	
Q99YN0_STRP1	M5005_Spy1335, SPy_1625	Serine/threonine protein kinase	5x10 <sup>-12</sup> - 1x10 <sup>-4</sup>	4/5	0/5	0/5	0/5	4/20	
Q9A156_STRP1	SPy_0457	Putative cyclophilin-type protein	7x10 <sup>-7</sup> - 2x10 <sup>-5</sup>	0/5	0/5	4/5	0/5	4/20	
EFTU_STRP1	<i>tuf</i> , SPy_0611, M5005_Spy0508	Elongation factor Tu	1x10 <sup>-14</sup> - 3x10 <sup>-11</sup>	3/5	0/5	0/5	0/5	3/20	
OTCC_STRP1	<i>arcB</i> , SPy_1544, M5005_Spy1273	Ornithine carbamoyltransferase, catabolic	2x10 <sup>-12</sup> - 8x10 <sup>-10</sup>	2/5	0/5	0/5	1/5	3/20	
PRSA1_STRP1	<i>prsA1</i> , SPy_1390, M5005_Spy1133	Foldase protein prsA 1	2x10 <sup>-12</sup> - 3x10 <sup>-11</sup>	3/5	0/5	0/5	0/5	3/20	
Q48ZN9_STRP1	<i>epf</i> , M5005_Spy0561	Putative extracellular matrix binding protein	1x10 <sup>-7</sup> - 2x10 <sup>-5</sup>	2/5	1/5	0/5	0/5	3/20	
Q99ZB3_STRP1	<i>amyA</i> , M5005_Spy1065, SPy_1302	Alpha-amylase	3x10 <sup>-15</sup> - 8x10 <sup>-5</sup>	3/5	0/5	0/5	0/5	3/20	
Q9A0A2_STRP1	M5005_Spy0678, SPy_0872	5'-nucleotidase	5x10 <sup>-9</sup> - 3x10 <sup>-5</sup>	2/5	1/5	0/5	0/5	3/20	
Q9A1H5_STRP1	<i>cbf</i> , M5005_Spy0227, SPy_0267	CMP-binding factor	7x10 <sup>-8</sup> - 3x10 <sup>-7</sup>	3/5	0/5	0/5	0/5	3/20	
LDH_STRP1	<i>ldh</i> , SPy_1151, M5005_Spy0873	L-lactate dehydrogenase	5x10 <sup>-9</sup> - 6x10 <sup>-5</sup>	2/5	0/5	0/5	0/5	2/20	
Q48WD4_STRP1	<i>isp</i> , M5005_Spy1723	Immunogenic secreted protein	6x10 <sup>-6</sup> - 7x10 <sup>-6</sup>	2/5	0/5	0/5	0/5	2/20	
Q48YT2_STRP1	<i>nox</i> , M5005_Spy0872	NADH oxidase H2O-forming	1x10 <sup>-8</sup> - 6x10 <sup>-8</sup>	2/5	0/5	0/5	0/5	2/20	
Q48Z64_STRP1	<i>cpsFQ</i> , M5005_Spy0736	dTDP-glucose 4,6-dehydratase	2x10 <sup>-7</sup> - 4x10 <sup>-4</sup>	2/5	0/5	0/5	0/5	2/20	
Q490V2_STRP1	M5005_Spy0247	Ribonuclease	8x10 <sup>-10</sup> - 4x10 <sup>-9</sup>	2/5	0/5	0/5	0/5	2/20	
Q99XV9_STRP1	<i>dppA</i> , M5005_Spy1704, SPy_2000	Dipeptide-binding protein	8x10 <sup>-7</sup> - 1x10 <sup>-6</sup>	2/5	0/5	0/5	0/5	2/20	
Q99YA0_STRP1	M5005_Spy1530, SPy_1798	Putative Fe3+-siderophore transport protein	2x10 <sup>-12</sup> - 2x10 <sup>-10</sup>	2/5	0/5	0/5	0/5	2/20	
Q99YA2_STRP1	M5005_Spy1528, SPy_1795	Ferrichrome-binding protein	6x10 <sup>-12</sup> - 8x10 <sup>-8</sup>	1/5	1/5	0/5	0/5	2/20	
Q99ZN4_STRP1	M5005_Spy0875, SPy_1154	Sortase	8x10 <sup>-8</sup> - 1x10 <sup>-6</sup>	1/5	0/5	0/5	1/5	2/20	
G6PI_STRP1	<i>pgi</i> , SPy_0215, M5005_Spy0185	Glucose-6-phosphate isomerase	6x10 <sup>-8</sup>	0/5	0/5	0/5	1/5	1/20	
Q48WD9_STRP1	<i>sic1.01</i> , M5005_Spy1718	Streptococcal inhibitor of complement	1x10 <sup>-30</sup>	1/5	0/5	0/5	0/5	1/20	
Q48X28_STRP1	<i>manL</i> , M5005_Spy1479	PTS system, mannose-specific IIB component	6x10 <sup>-11</sup>	1/5	0/5	0/5	0/5	1/20	
Q7DAL3_STRP1	<i>scl</i> , <i>sclA</i> , M5005_Spy1687, SPy_1983	Collagen-like surface protein	1x10 <sup>-7</sup>	1/5	0/5	0/5	0/5	1/20	
Q7DAM2_STRP1	<i>mac</i> , M5005_Spy0668, SPy_0861	IgG-degrading protease	7x10 <sup>-11</sup>	1/5	0/5	0/5	0/5	1/20	
Q99Z26_STRP1	<i>mf3</i> , SPy_1436	Putative deoxyribonuclease	4x10 <sup>-10</sup>	1/5	0/5	0/5	0/5	1/20	
Q99Z67_STRP1	<i>gapN</i> , M5005_Spy1119, SPy_1371	NADP-dependent glyceraldehyde-3-phosphate dehydrogenase	3x10 <sup>-8</sup>	1/5	0/5	0/5	0/5	1/20	
Q99ZU1_STRP1	M5005_Spy0793, SPy_1070	Putative dipeptidase	2x10 <sup>-9</sup>	0/5	0/5	0/5	1/5	1/20	
Q99ZX5_STRP1	<i>acol</i> , M5005_Spy0755, SPy_1031	Dihydroliipoamide dehydrogenase	6x10 <sup>-4</sup>	1/5	0/5	0/5	0/5	1/20	
Q9A1E5_STRP1	M5005_Spy0270, SPy_0317	ABC transporter substrate-binding protein	9x10 <sup>-7</sup>	0/5	0/5	1/5	0/5	1/20	
Q9A068_STRP1	<i>bcaT</i> , M5005_Spy0713, SPy_0911	Branched-chain-amino-acid aminotransferase	6x10 <sup>-6</sup>	1/5	0/5	0/5	0/5	1/20	
Q9A146_STRP1	SPy_0470	67 kDa Myosin-crossreactive streptococcal antigen	9x10 <sup>-6</sup>	1/5	0/5	0/5	0/5	1/20	
Q9A1E4_STRP1	M5005_Spy0271, SPy_0319	ABC transporter substrate-binding protein	1x10 <sup>-6</sup>	0/5	0/5	0/5	1/5	1/20	
RPOA_STRP1	<i>rpoA</i> , SPy_0080, M5005_Spy0070	DNA-directed RNA polymerase subunit alpha	6x10 <sup>-6</sup>	1/5	0/5	0/5	0/5	1/20	
SYA_STRP1	<i>alaS</i> , SPy_1389, M5005_Spy1132	Alanyl-tRNA synthetase	1x10 <sup>-5</sup>	1/5	0/5	0/5	0/5	1/20	
SYS_STRP1	<i>serS</i> , SPy_1742, M5005_Spy1483	Seryl-tRNA synthetase	2x10 <sup>-10</sup>	1/5	0/5	0/5	0/5	1/20	
Y652_STRP1	SPy_0652, M5005_Spy0539	UPF0042 nucleotide-binding protein	9x10 <sup>-10</sup>	1/5	0/5	0/5	0/5	1/20	

<25%

**Supplementary Table 3: The *S. pyogenes* antigens purified by comparative immunoprecipitation.** Numbers represent the proportion of strains from which targets were identified. Targets identified from  $\geq 75\%$  of strains using one or more E-IVIG preparations are displayed.

Uniprot Identifier	Protein product	Endobulin					Intratect					Privigen				
		M1	M12	M3	M89	Total	M1	M12	M3	M89	Total	M1	M12	M3	M89	Total
C5AP_STRP1	C5a peptidase	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
DNAK_STRP1	Chaperone protein DnaK	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
EFTS_STRP1	Elongation factor Ts	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
MTSA_STRP1	Metal ABC transporter substrate-binding lipoprotein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
PGK_STRP1	Phosphoglycerate kinase	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q48Y96_STRP1	Maltose/maltodextrin-binding protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q490V0_STRP1	Oligopeptide-binding protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q491G2_STRP1	Nucleoside-binding protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q7DAN2_STRP1	Nicotine adenine dinucleotide glycohydrolase	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q99XX8_STRP1	Putative pullulanase	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q99ZH4_STRP1	Nucleoside-binding protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q99ZW9_STRP1	Hypothetical membrane associated protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q9A0C0_STRP1	Cell surface protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q9A0J7_STRP1	Endonuclease/exonuclease/phosphatase family protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q9A1G0_STRP1	Penicillin-binding protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q9A1H3_STRP1	SpyAD	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
Q9A1Z8_STRP1	Putative secreted protein	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8
TACY_STRP1	Streptolysin O	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8	2/2	2/2	2/2	2/2	8/8

**Supplementary Table 3 continued:**

Uniprot Identifier	Protein product	Endobulin					Intratect					Privigen				
		M1	M12	M3	M89	Total	M1	M12	M3	M89	Total	M1	M12	M3	M89	Total
G3P_STRP1	Glyceraldehyde-3-phosphate dehydrogenase	1/2	2/2	2/2	2/2	7/8	1/2	2/2	2/2	2/2	7/8	1/2	2/2	2/2	2/2	7/8
PILIN_STRP1	Pilin	2/2	2/2	2/2	1/2	7/8	2/2	2/2	2/2	1/2	7/8	2/2	2/2	2/2	1/2	7/8
Q490K8_STRP1	SpyCEP	1/2	2/2	2/2	2/2	7/8	1/2	2/2	2/2	2/2	7/8	1/2	2/2	2/2	2/2	7/8
Q99XV0_STRP1	M protein type 1	2/2	2/2	2/2	1/2	7/8	2/2	2/2	2/2	1/2	7/8	2/2	2/2	2/2	1/2	7/8
Q99ZT1_STRP1	Polysaccharide deacetylase	2/2	2/2	1/2	2/2	7/8	2/2	2/2	1/2	2/2	7/8	2/2	2/2	1/2	2/2	7/8
Q9A156_STRP1	Putative cyclophilin-type protein	1/2	2/2	2/2	2/2	7/8	1/2	1/2	2/2	1/2	5/8	2/2	2/2	1/2	2/2	7/8
PEPDB_STRP1	Probable dipeptidase B	2/2	1/2	1/2	2/2	6/8	2/2	1/2	2/2	1/2	6/8	2/2	1/2	1/2	2/2	6/8
Q99XV4_STRP1	Streptococcal histidine triad protein	2/2	1/2	1/2	2/2	6/8	2/2	1/2	0/2	2/2	5/8	2/2	1/2	1/2	1/2	5/8
Q99YL6_STRP1	Putative uncharacterized protein	1/2	1/2	1/2	2/2	5/8	2/2	1/2	0/2	2/2	5/8	1/2	2/2	1/2	2/2	6/8
Q9A0C5_STRP1	Putative uncharacterized protein	2/2	0/2	1/2	2/2	5/8	2/2	0/2	1/2	1/2	4/8	2/2	2/2	1/2	2/2	7/8
Q99XU2_STRP1	Periplasmic component of efflux system	1/2	1/2	0/2	2/2	4/8	0/2	1/2	0/2	2/2	3/8	2/2	1/2	2/2	2/2	7/8
Q9A147_STRP1	Putative 42 kDa protein	0/2	1/2	2/2	0/2	3/8	2/2	2/2	2/2	1/2	7/8	0/2	2/2	2/2	0/2	4/8



