

Protein	CASP target	Chemistry	Protein concentration (mg/mL)	Incubation time (min)	Incubation temp. (°C)	Buffer
<b>CDI209</b>	<b>X0957</b>	DSS	0.25	30	25	50 mM HEPES/Na pH 7.8, 150 mM NaCl and 2 mM DTT
		PDH	1	30	25	50 mM HEPES/Na pH 7.8, 150 mM NaCl and 2 mM DTT
<b>CDI213</b>	<b>X0968</b>	DSS	0.25	30	25	50 mM HEPES/Na pH 7.8, 150 mM NaCl and 2 mM DTT
		PDH	1	30	37	50 mM HEPES/Na pH 7.8, 150 mM NaCl and 2 mM DTT
<b>ETH</b>	<b>X0953</b>	DSS	1	30	25	20 mM HEPES pH 7.5
		PDH	1	30	25	20 mM HEPES pH 7.5
<b>gp146</b>	<b>X0981</b>	DSS	1	30	25	10 mM Tris-HCl pH 8.5 > exchanged to 20 mM Hepes pH 8.5, 150 mM NaCl
		PDH		Not performed		
<b>Esp405</b>	<b>X0987</b>	DSS	1	30	25	PBS buffer pH 7.4
		PDH	1	30	25	PBS buffer pH 7.4
<b>Exo5</b>	<b>X0975</b>	DSS	1	30	25	50 mM HEPES, pH 7.5, 300 mM NaCl, 0.5 mM TCEP, 3% glycerol
		PDH	1	30	25	50 mM HEPES, pH 7.5, 300 mM NaCl, 0.5 mM TCEP, 3% glycerol
<b>ACL_1061</b>	<b>X0985</b>	DSS	0.5	30	25	20 mM HEPES pH 7.5, 50 mM NaCl, 1 mM DTT
		PDH	1	30	25	20 mM HEPES pH 7.5, 50 mM NaCl, 1 mM DTT
<b>AROM</b>	<b>X0999</b>	DSS	1	30	37	20 mM HEPES pH 8.0, 150 mM NaCl, 2 mM TCEP, 1% sucrose, 15% glycerol
		PDH		Not performed		

**Supplementary Table 1.** Experimental conditions for crosslinking experiments in BigX group.