

**Supplementary Table 1. Data collection and refinement statistics for MLCK1 IgCAM3 crystal structure\*.**

MLCK1 IgCAM3	
<b>Data collection</b>	
Space group	P6 <sub>5</sub>
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	74.69, 74.69, 131.48
$\alpha$ , $\beta$ , $\gamma$ (°)	90.0, 90.0, 120.0
Resolution (Å)	46 – 2.5 *
<i>R</i> <sub>sym</sub> or <i>R</i> <sub>merge</sub>	0.076 (0.879)
<i>I</i> / $\sigma I$	13.2 (2.1)
Completeness (%)	98.8 (99.9)
Average redundancy	6.2
<b>Refinement</b>	
Resolution (Å)	46 – 2.5
No. reflections (working/test)	14404 / 2842
<i>R</i> <sub>cryst</sub> / <i>R</i> <sub>free</sub> (%)	22.6 / 27.2
No. atoms	
Protein	2247
Ligand/ion	N/A
Water	57
<i>B</i> -factors	
Protein	81
Ligand/ion	N/A
Water	60
R.m.s. deviations	
Bond lengths (Å)	0.011
Bond angles (°)	1.43

\*Data were collected from a single crystal. \*Values in parentheses are for highest-resolution shell.

**Supplementary Table 2. Summary of biological screen results**

<b>NSC number</b>	<b>Transepithelial resistance</b>	<b>Kinase activity</b>	<b>Gel contraction</b>
351093	no effect		
42233	no effect	inhibition	Inhibition
31211	increased	no effect	Inhibition
14010	no effect		
159456	increased	inhibition	no effect
353874	no effect		
51344	decreased	no effect	no effect
91855	no effect		
<b>55937</b>	<b>increased</b>	<b>no effect</b>	<b>no effect</b>
134514	no effect		
641058	no effect		
294786	no effect	inhibition	inhibition
48770	no effect	no effect	inhibition
34629	no effect		
68361	no effect	inhibition	no effect
267461	no effect		
122301	no effect		