## **Supporting Information**

## **Top-Down Analysis of In-Source HDX of Native Protein Ions**

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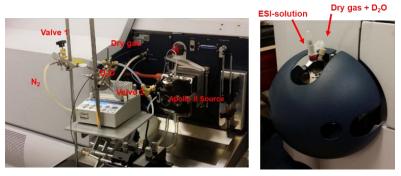


Figure S1. Pictures and Schematic of modified gas inlet system.

	[ <b>M+6H</b> ] <sup>6+</sup>	[ <b>M+8H</b> ] <sup>8+</sup>	[ <b>M+11H</b> ] <sup>11+</sup>
Control	1/100 1/400 (0001)	100 min 100 mi	787 788 782 5065 779 780 781 782 5065 781 5062
1.5 L/min	+11 Da	+17 Da	+14 Da
2.0 L/min	+11 Da	+17 Da	+13 Da
2.5 L/min	+12 Da	+17 Da	+12.Da
3.0 L/min	+10 Da	+15 Da	+10 Da
4.0 L/min	+7 Da	+11 Da	+7 Da
5.0 L/min	+8 Da	+13 Da	+9 Da
6.0 L/min	+7 Da	+10 Da	+8,Da
7.0 L/min	+6 Da	+10 Da	+7 Da

Figure S2. Effect of dry gas (N<sub>2</sub>) flow rate on HDX of ubiquitin.

	[M+6H] <sup>6+</sup>	[M+8H] <sup>8+</sup>	[M+11H] <sup>11+</sup>
Control	1428-7105	1071,7663	779 7293
50 °C	+13 Da	1074 0448 +18 Da	781 0167 + <b>14 Da</b>
100 °C	1430.4722 +11 Da	1074.3710 +21 Da	780 9025 <b>+13 Da</b>
150 °C	+11 Da	+18 Da	779 1837 779 1837
180 °C	+13 Da	1074.3956 +21 Da	<sup>700 9154</sup> +13 Da
200 °C	+10 Da	1073.0134 +17 Da	779.2012 779.2012 <b>+13 Da</b>
250 °C	+13 Da	+16 Da	+11 Da
300 °C	1431 2588 + <b>15 Da</b>	+ <b>15</b> Da	+11 Da
350 °C	+141 Da	+15 Da	780 5819 +9 Da

Figure S3. Effect of dry gas  $(N_2)$  temperature on HDX of ubiquitin.

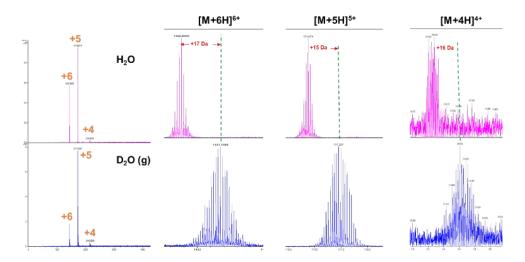


Figure S4. Deuterium uptake as a function of charge state of native ubiquitin ions. There is no difference in solvent accessibility of different charge states of native ubiquitin.