Supplementary information Van Wijk et al.

Supplementary Table I
Overview of human ubiquitin-conjugating enzymes (MS Excel spreadsheet document (.xls))

Supplementary Table II
Overview of human RING-type E3 ligases (MS Excel spreadsheet document (.xls))

Supplementary Table III
Overview of binary human E2-E3 interactions (Tab-delimited text document (.txt))

Supplementary Table IV
Overview of all background-corrected E2-E3 interactions detected on LacZ-staining (Tab-delimited text document (.txt))

Supplementary Table V
Overview of all background-corrected E2-E3 interactions detected on LEU2-auxotrophy (Tab-delimited text document (.txt))

Supplementary Table VI
Overview of observed E2-E3 interactions compared with literature-curated, biochemically functional interactions (MS Excel spreadsheet document (.xls))

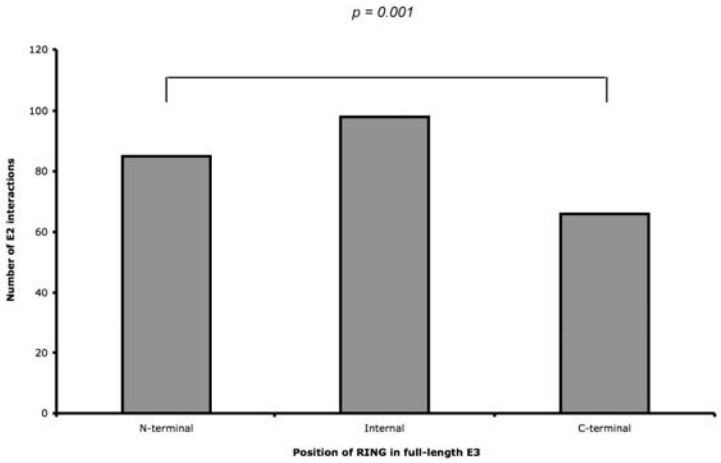
Supplementary Figure 1
Influence of RING-domain position relative to the full-length E3 protein on E2 interacting potential (Portable Document Format document (.pdf))

Supplementary Figure 2
Network robustness (Portable Document Format document (.pdf))

Supplementary Figure 3
Hub overlap index (Portable Document Format document (.pdf))

Supplementary Figure 4
E2 similarity indices (Portable Document Format document (.pdf))

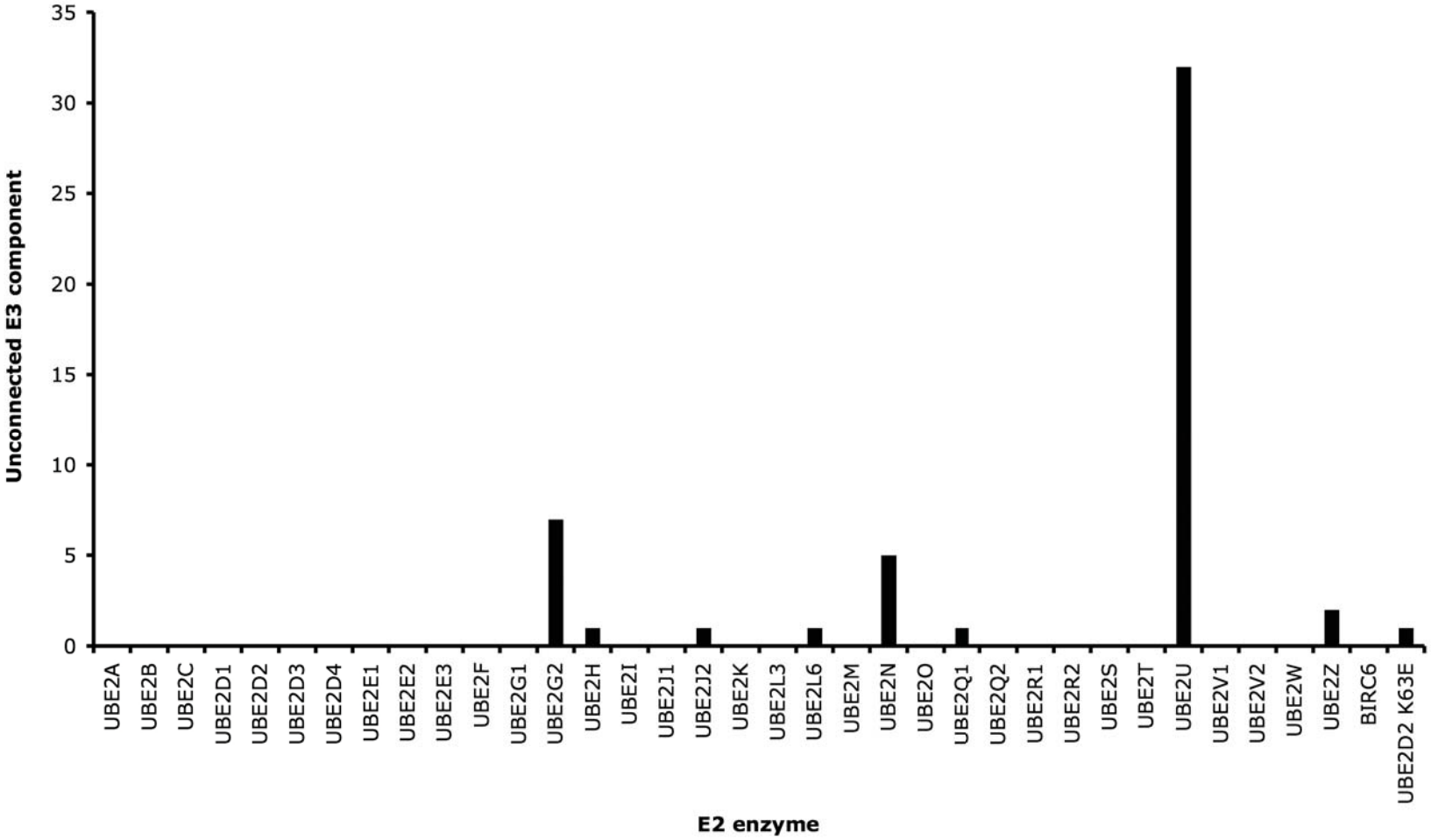
Number of E3 interactions	E2 N-terminal	E2 Internal	E2 C-terminal	
0	48	66	31	
1	27	12	12	
2	5	3	6	
3	3	2	1	
4	1	0	2	
5	0	1	1	
6	1	0	3	
7	0	2	3	
8	0	6	2	
9	0	4	3	
10	0	1	2	
11	0	1	0	Total
Total E3	85	98	66	249
Total E2 interactions (≥ 0)	56	148	142	346



Supplementary Figure 1

Influence of RING-domain position relative to the full-length E3 protein on E2 interaction potential Importance of E3-connections of individual E2 nodes in the E2-E3 ubiquitination interaction network for system robustness. Individual E2 nodes were deleted from the network, followed by quantification of the number of unconnected E3s, as measure for the system's fidelity.

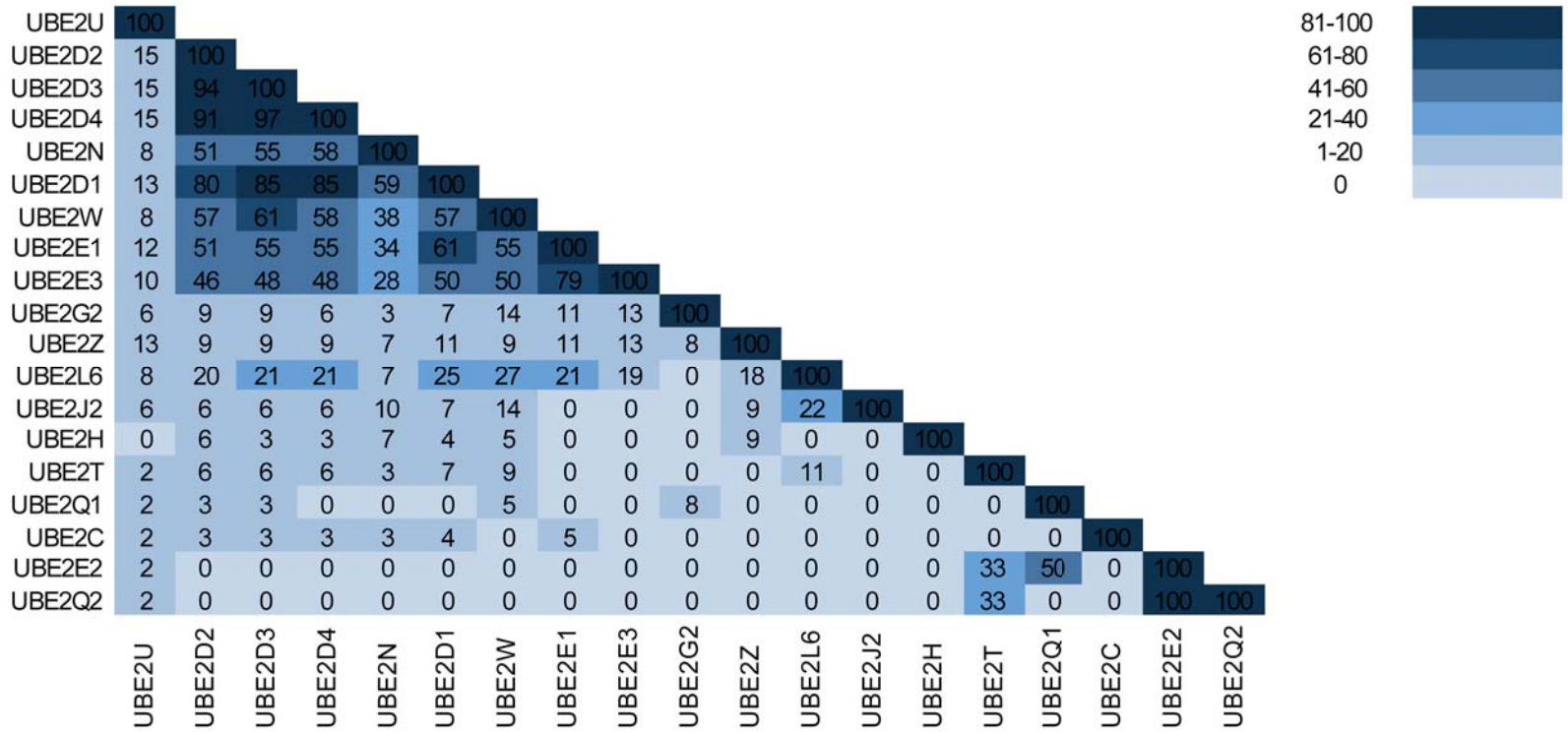
VanWijk_SuppFig_1



Supplementary Figure 2

Network robustness Importance of E3-connections of individual E2 nodes in the E2-E3 ubiquitination interaction network for system robustness. Individual E2 nodes were deleted from the network, followed by quantification of the number of unconnected E3s, as measure for the system's fidelity.

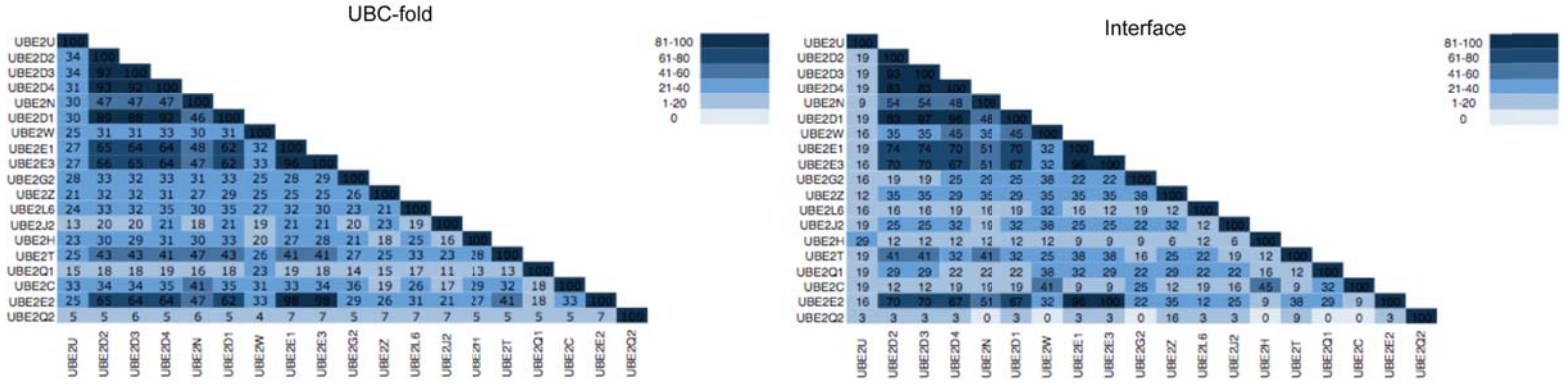
VanWijk_SuppFig_2



Supplementary Figure 3

Hub overlap index Shared E3 binding partners were calculated for each E2 showing more than one interaction.

VanWijk_SuppFig_3



Supplementary Figure 4

E2 similarity indices Percentages sequence identity between all human E2 nodes in the E2-E3 network showing more than one interaction, displayed over the complete UBC-fold (*left*) or the predicted E3-binding interface, as determined by the CNOT4-UbcH5B model (PDB-code: 1UR6; *right*).

VanWijk_SuppFig_4