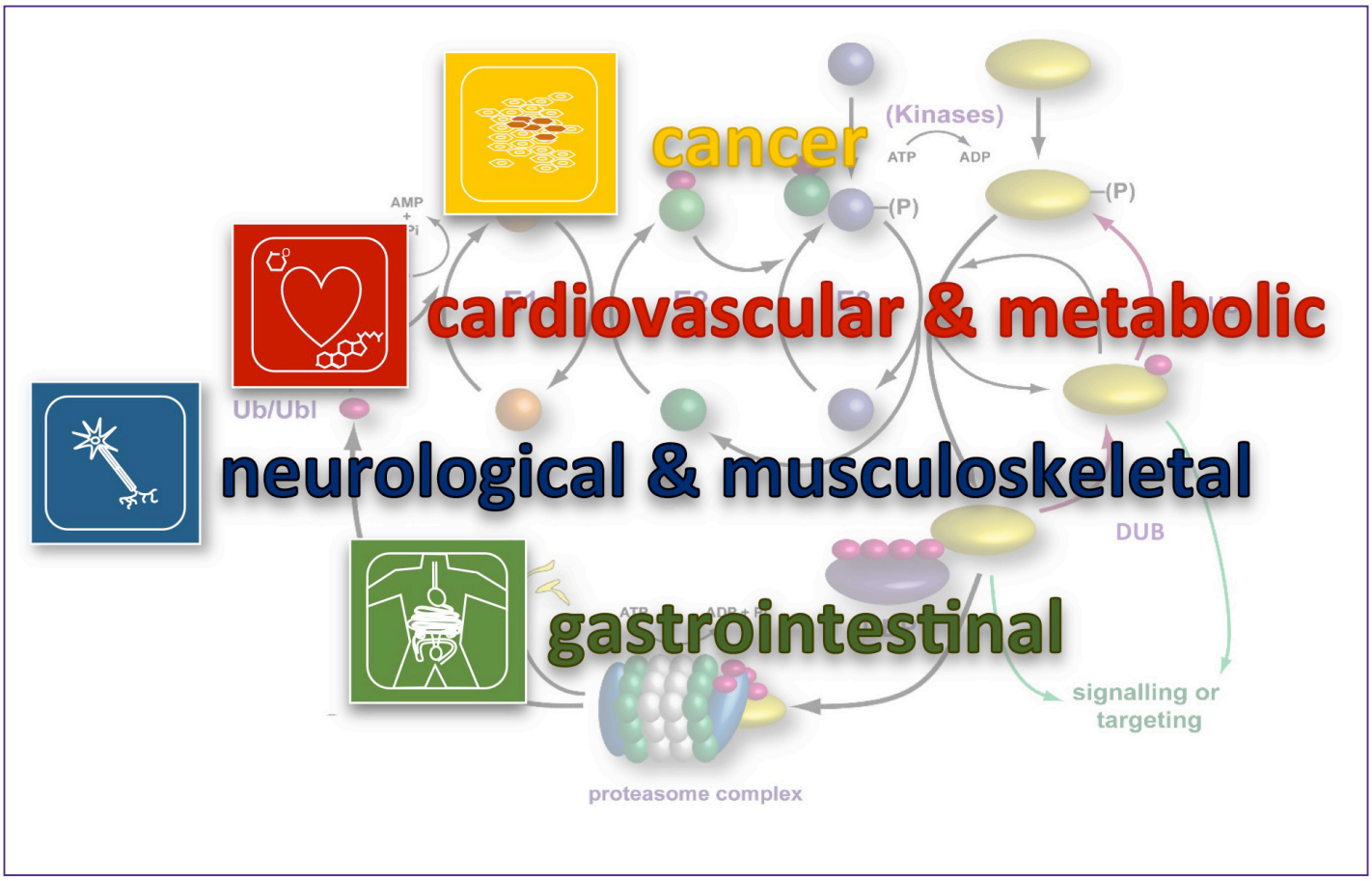
UBIQUInews

The Newsletter of **Ubiquigent Ltd.** Number 1 February 2014



INSIDE:

NEW - Therapeutic Areas and the Ubiquitin System

For researchers considering the ubiquitin system as a potential new route to investigating disease mechanisms, and possibly a new source of drug discovery targets to consider, we present a guide and a resource to enable you to begin identifying and grouping such associations.

A growing number of excellent reviews are being published, which offer well-referenced summaries of work in particular disease areas, pathways or amongst the members of certain ubiquitin system protein families.

At Ubiquigent we have started collecting such information and collating target lists with disease associations, choosing to group the proteins into four interconnected therapeutic areas: Oncology, Cardiovascular, inflammatory and metabolic, Neurological and musculoskeletal, and Gastrointestinal, hepatic and renal. You may have spotted these on our website already.

As the pathways and networks of cell signalling are revealed, our understanding of the variety and complexity of protein modifications that regulate cellular functions continues to grow. The critical role that the ubiquitin cascade plays in cellular signalling and protein homeostasis, coupled with increasing validation of the therapeutic potential of targets in this pathway is accelerating interest in ubiquitin system-targeted drug discovery.

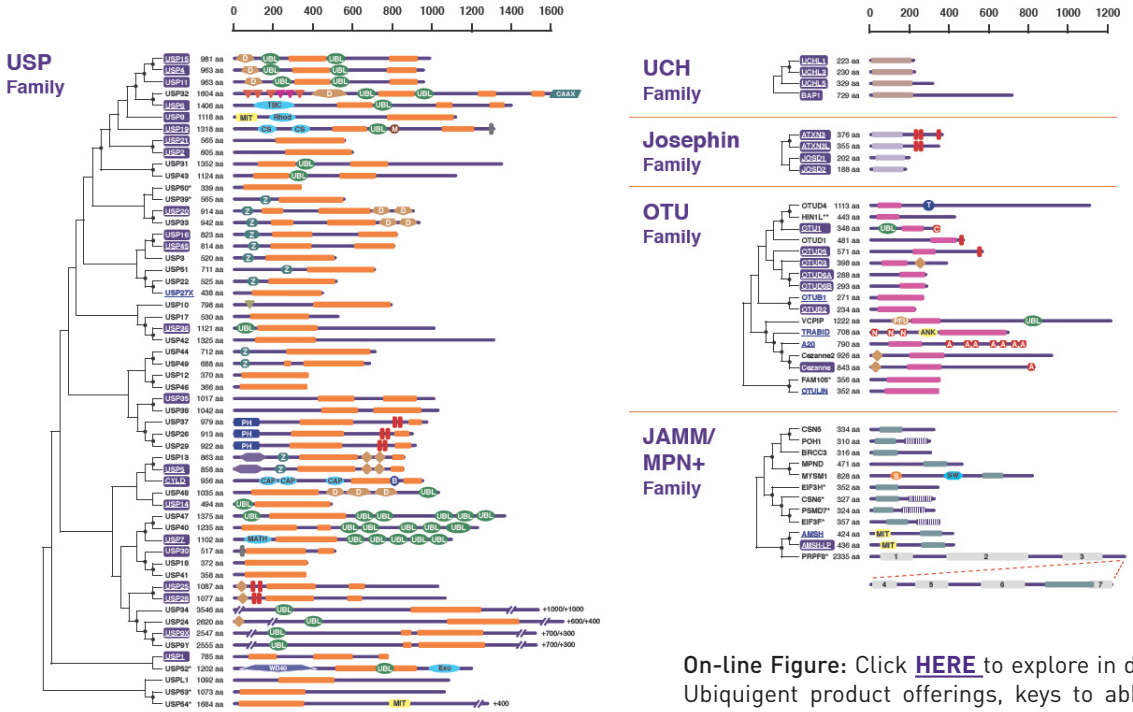
In this section of the website, we have sought to begin assembling proteins of the ubiquitin system into four groups according to their connections with key therapeutic areas. This is not intended to be an exhaustive list but one that highlights some of the most recent work across a variety of therapeutic areas, and one that adds weight to the notion of various ubiquitin system proteins as potentially attractive new targets for drug discovery.

As with any such exercise the lists so created cannot claim to be complete, and can be updated only as frequently as time and resources permit. Their purpose however is to provide some insights regarding the rich and growing opportunity for ubiquitin system-targeted drug discovery. Ubiquigent and their scientific advisors and collaborators have added their support to this endeavour and we will continue to build this online resource, and hope that you will help us too.

Do tell us about ubiquitin system disease associations and targeting opportunities that you have published on via **this link** and create a link to our Therapeutic Area pages from your own website.

NEW - The Human DUB Superfamily

Presented below are a set of phylogenetic trees representing the human deubiquitylating (DUB) enzyme superfamily. The families were constructed by homology alignment of the de-ubiquitylating catalytic domain sequences of the enzymes. Further enzyme architecture is indicated as predicted from domain (CDD, HHsearch, Pfam and SMART) and structure (PDB) databases. This tree and legend are presented with the permission of Prof. Michael Clague and Prof. Sylvie Urbé at the Institute of Translational Medicine, and Institute of Integrative Biology, University of Liverpool, UK.



On-line Figure: Click **HERE** to explore in detail. You will find Ubiquigent product offerings, keys to abbreviations, references and a link to a 2-page print-friendly version.

TOBIAS WINTER – Winner of the Ubiquigent Young Scientist Prize, 2013

Ubiquigent is delighted to announce that Tobias Winter was awarded the Ubiquigent Young Scientist Prize at the Cold Spring Harbor Laboratories (CSHL) meeting on 'The Ubiquitin Family' held at CSHL, Long Island, NY, USA in May 2013.

Mr. Winter was selected to receive the award by the prize-giving committee for his poster entitled "The RanBP2 complex and Crm1 – a tight embrace", and was presented with the award by Professor Brenda Schulman of St. Jude Children's Research Hospital, TN, USA, one of the meeting co-organisers.

Ubiquigent's Managing Director Dr Jason Brown commented; "Ubiquigent was delighted to continue our sponsorship of a Young Scientist Prize – this year in collaboration with the Cold Spring Harbor Laboratories ubiquitin meeting – and congratulate Tobias Winter on being selected by the prize committee."

Cullin Ring Ligases

The cullin-RING ubiquitin ligases (CRLs) are a superfamily of multi-component RING-E3 complexes that comprise a cullin scaffold protein and a catalytic RING subunit, Rbx1 or Rbx2. To date, seven closely related cullin proteins, Cul1, Cul2, Cul3, Cul4A, Cul4B, Cul5 and Cul7 have been identified. The cullin proteins exist in complex with Rbx1 or Rbx2 and form different subfamilies of CRLs, CRL1–CRL5 (Figure 1). The largest of these families the Skp1-Cullin1 (Cul1)-F-Box Protein (FBP) (SCF) ligases, comprise an adaptor protein Skp1 which forms a bridge between Cul1 and an FBP. The FBP is responsible for binding the substrate and is referred to as the specificity factor while Rbx1 recruits ubiquitin-loaded E2 conjugating enzyme which - as part of the CRL complex - enables ubiquitylation of the substrate (Bennet *et al.*, 2010; Zimmerman *et al.*, 2010; Lydeard *et al.*, 2013).

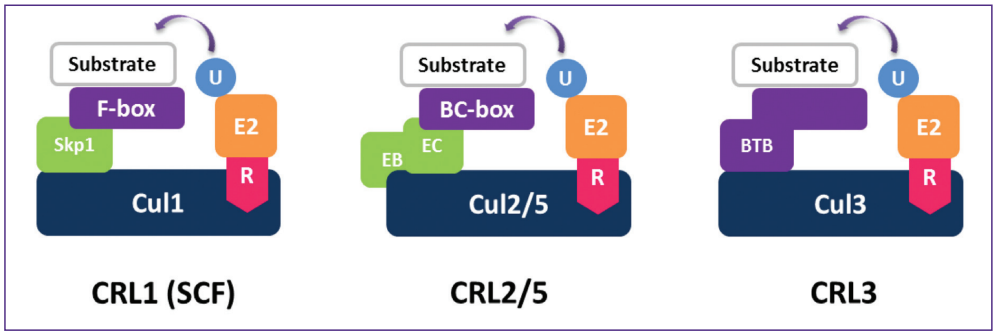


Figure 1: Cullin scaffold proteins (Cul1, Cul2/5 and Cul3): Dark blue box; Rbx1/2 (R): Red arrow; Ubiquitin (U)-charged E2 enzymes (E2): orange box with light blue circle; Skp1, Elongin C (EC) and Elongin B (EB) adaptor proteins (green box); F-box, BC-box, BTB-domain proteins substrate receptors (purple box). (Modified from Zimmerman *et al.*, 2010)

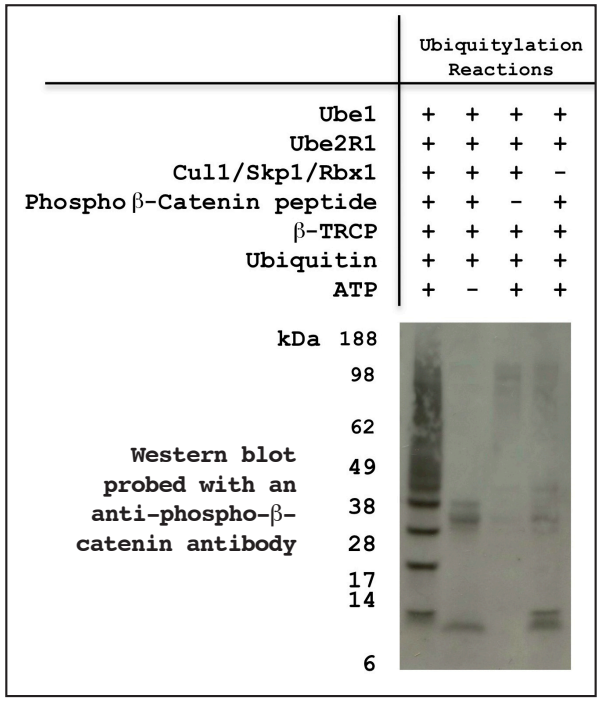


Figure 2: Cul1/Rbx1/Skp1 catalysed phospho β-Catenin Ubiquitylation: The activity of Cul1/Skp1/Rbx1 was validated through its ability to catalyse the generation of polyubiquitin chains in the presence of the E1 activating enzyme His-Ube1, the E2 conjugating enzyme His-Ube2R1, ubiquitin, the F-box protein Beta-Transducin Repeat Containing Protein (βTrCP), and the substrate phospho-β-Catenin. Incubation of a reaction for 60 minutes at 30˚C containing His-Ube1, His-Ube2R1, ubiquitin, Cul1/Skp1/Rbx1, β-TrCP, phospho-β-Catenin and ATP was compared alongside three control reactions with either ATP, phospho-β-Catenin, or Cul1/Skp1/Rbx1 excluded from the reaction. Analysis of these reactions by Western blotting using an anti-phospho-β-Catenin antibody identified ubiquitylated phospho-β-Catenin substrate only in the presence of both ATP and Cul1/Skp1/Rbx1.

The cullin proteins have been associated with a number of human diseases such as Alzheimer's Disease, Rheumatoid Arthritis, Leukaemia as well as gastric, renal and bladder cancers. For more information on these associations visit the new **Therapeutic Areas and the Ubiquitin System** section on the Ubiquigent website.

Ubiquigent now offers a number of purified Cullin heterodimers and a heterotrimer as part of a growing portfolio of E3 ubiquitin ligases to help facilitate your research.

CRL	Cat. No.
Cul1/Rbx1 [untagged]	63-1000-025
Cul1/Rbx1/Skp1 [untagged]	63-1001-025
Cul3/Rbx1 [untagged]	63-1003-025
Cul5/Rnf7 [untagged]	63-1002-025

(25 microgram pack size)

References:

Zimmerman ES, Schulman BA, Zheng N. (2010) Structural assembly of cullin-RING ubiquitin ligase complexes. *Curr Opin Struct Biol.* **20** 714-21.

Bennett EJ, Rush J, Gygi SP, Harper JW. (2010) Dynamics of cullin-RING ubiquitin ligase network revealed by systematic quantitative proteomics. *Cell.* **143** 951-65.

Lydeard JR, Schulman BA, Harper JW. (2013) Building and remodelling Cullin-RING E3 ubiquitin ligases. *EMBO Rep.* **14** 1050-61.

The growing story of ubiquitin binding protein selectivity

*Commentary on a review article from Prof. Philip Cohen's lab **

A recent review from Clark* *et al.* has brought together much experimental evidence and current thinking regarding the modes of action of the NF-κB essential modulator (NEMO; also known as IKKγ). This review also points towards a developing picture about the significance of the ubiquitin binding functions of NEMO and other related proteins, in particular their selectivity for ubiquitin chain types, and their resulting roles in different cellular events.

** Medical Research Council (MRC) Protein Phosphorylation and Ubiquitylation Unit, Sir James Black Centre, University of Dundee.*

The central role of NEMO in the innate immune system is made clear through knowledge of its control of the activation of the canonical IKK complex, its directing of IKKs to their physiological substrates and its regulation of IKK-related kinases. NEMO and other ubiquitin-binding proteins display an emerging range of selectivity for polyubiquitin and ubiquitin dimers which, when linked in different ways adopt unique architectures, enabling specific recognition of signalling 'codes' by distinct sets of ubiquitin-binding proteins.

NEMO itself has specificity for Met1 and Lys63 linked ubiquitin dimers, each resulting in different but related roles in IL-1, TNF and lipopolysaccharide signalling.

Perhaps of broader biological significance though are the analogies that could be drawn from NEMO's functions, since NEMO and Lys63-linked and Met1-linked ubiquitin chains have also been implicated in the regulation of many processes, such as the cellular response to DNA damage.

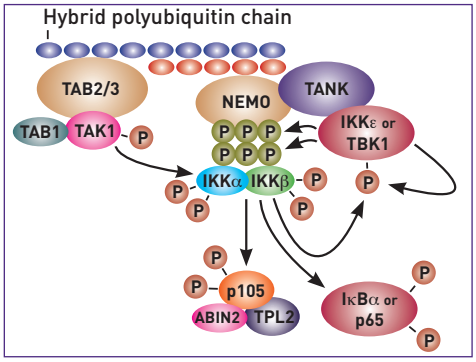


Figure: NEMO interacts with NF-κB activator (TANK), forming a complex comprising both canonical IκB kinases (IKKs; IKKα and IKKβ) and IKK-related kinases. (adapted from Clark *et al.* (2013))

Clark *et al.* (2013) also summarises work on NEMO's relatives ABIN1 (A20-binding inhibitor of NF-κB), ABIN2, ABIN3 and optineurin (OPTN; also known as NEMO-related protein). These all share related ubiquitin-binding domains, and like NEMO, also regulate – and in some cases are themselves regulated by – protein kinases. More investigation is required to further elucidate poly- and di-ubiquitin specificities, and to link those properties to their biological functions.

Reference:

Clark K, Nanda S and Cohen P (2013) Molecular control of the NEMO family of ubiquitin-binding proteins. *Nature Reviews. Cancer*, **13**, 673-685.

Product Name	Description	Cat. No.	Pack
NEMO [GST-tagged]	Human recombinant protein	66-1002-050	50 µg
NEMO (D311N) [GST-tagged]	Ubiquitin binding-deficient mutant	66-1013-050	50 µg
Optineurin [GST-tagged]	Human recombinant protein	66-1005-050	50 µg
Optineurin (D474N) [GST-tagged]	Ubiquitin binding-deficient mutant	66-1014-050	50 µg
A20 CD(1-366) [GST-tagged]	Forms complex with NEMO and polyubiquitin in NF-κB signalling	64-0047-050	50 µg
TBK1 [GST-tagged]	Phosphorylates NEMO in response to IL-1 signalling	66-0016-050	50 µg
TAK1_TAB1 complex [6His-tagged]	Regulated by Lys63 binding TAB2/3 in activation of the canonical IKK complex	66-0007-050	50 µg
Di-ubiquitin (K63-linked) [untagged]	Here referred to as Lys63-linked	60-0107-050 60-0107-010	50 µg 10 µg
Di-ubiquitin (K48-linked) [untagged]	Here referred to as Lys48-linked	60-0106-050 60-0106-010	50 µg 10 µg
Di-ubiquitin (linear) [GST-cleaved]	Here referred to as Met1-linked	60-0115-050 60-0115-010	50 µg 10 µg

NEW - DUB*profiler*™ Version 5 Upgrades

Ubiquigent recently launched the latest expansion of its DUB*profiler* service, taking the number of individual DUB targets to 38 and expanding the total panel of assays now available for profiling and screening to 42. The most recent additions are indicated, and the rationale for their inclusion is presented below. We continue to work on new additions, and as always welcome your suggestions. You may also be interested in finding out more about these and other ubiquitin system targets and their disease associations; visit the new Therapeutic Areas and the Ubiquitin System resource on the Ubiquigent website.

USP5 (+Ub@Kd) & USP5 (+Ub@Bmax)

In addition to the current offering of USP5 on our DUB*profiler* panel, we now offer a further two USP5 screening options. There is evidence in both the literature and from our in-house experiments that USP5's catalytic activity can itself be activated by ubiquitin. USP5 contains an N-terminal zinc finger ubiquitin-binding domain (ZNF-UBP), a ubiquitin-specific processing protease domain containing the active-site Cys and His boxes, and two ubiquitin-associated domains (UBA1 and UBA2). Crystal structures of the ZNF-UBP domain have revealed a deep binding pocket where the C-terminal diglycine motif of ubiquitin is inserted explaining the specificity of USP5 for an unmodified C-terminus on the proximal subunit of polyubiquitin. Mutations in this domain demonstrate that it is required for the optimal catalytic activation of USP5 (Reyes-Turcu *et al.*, 2006). Our DUB*profiler* version 5 upgrade now offers the additional options of screening USP5 in the presence of ubiquitin at either a concentration that binds to half of the ZNF-UBP receptor sites at equilibrium (Kd) or at a concentration above the maximal binding capacity (Bmax). This choice of screening options for inhibitors of USP5 offers a deeper level of investigation and understanding of the compound's mechanism of action. Thus for example screening USP5 in the presence of ubiquitin at Kd – rather than at Bmax – with respect to USP5 activation makes the assay more sensitive to (allosteric) inhibitors of USP5's catalytic activity that bind to the ubiquitin-mediated ZNF-UBP activation site on the enzyme. ►►

USP Family Accession #s	
USP1/UAF1	NP_003359 / NP_065890
USP2	NP_741994
USP4	NP_003354
USP5	P45974
USP5 (+Ub@Kd)	P45974
USP5 (+Ub@Bmax)	P45974
USP6	NP_004496
USP7	CAA96580
USP8	NP_005145
USP9x	NP_001034680
USP11	NP_004642
USP14 (+Ptsm-VS@Kd)	AAH03556
USP15	NP_006304
USP16	AAH30777
USP19	NP_006668
USP20	AAH39593
USP21	NP_001014443
USP25	NP_037528
USP28	NP_065937
USP30	NP_116052
USP35	NP_065849
USP36	AAH27992.1
USP45	NP_001073950
CYLD	NP_056062

OTU Family Accession #s	
OTU1	NP_061036
OTUB2	NP_075601.1
OTUD3	NP_056022
OTUD5 (p177S)	AAH09917
OTUD6A	NP_997203
OTUD6B	NP_057107
Cezanne	NP_064590

JAMM Family Accession #s	
AMSH-LP	NP_065850
AMSH-LP (+Zinc)	NP_065850

Josephin Family Accession #s	
Ataxin3	AAH33711
Ataxin3L	NP_001129467
JOSD1	NP_055691
JOSD2	NP_612207

UCH Family Accession #s	
UCHL1	AAH00332
UCHL3	A AH18125
UCHL5	AAH15521.1
BAP1	AAH01596.1

USP8

USP8 regulates the degradation of various transmembrane proteins at the sorting endosome by modulating the ubiquitin dynamics of both cargo and sorting proteins. USP8 interacts with signal transducing adaptor molecule (STAM) and stabilizes STAM and hepatocyte growth factor-regulated substrate (Hrs), which together constitute the endosomal sorting complex required for transport (ESCRT) and governs the early steps of receptor trafficking en route to the lysosomes (De Ceuninck *et al.*, 2013). The E3 ubiquitin ligase IDOL (inducible degrader of the LDLR) employs ESCRT complexes to recognise and traffic low-density lipoprotein receptor (LDLR) to lysosomes (click **here** to access Ubiquigent's IDOL HTS assay). IDOL is recruited to the plasma membrane by LDLR, promoting LDLR internalisation and facilitating LDLR degradation by shuttling it into the multivesicular body (MVB) protein-sorting pathway. USP8 acts downstream of IDOL to deubiquitylate LDLR and is required for LDLR entry into the MVB pathway (Scotti *et al.*, 2013; Sorrentino *et al.*, 2013). USP8 has also been shown to interact with and stabilise the E3 ubiquitin ligase Ring Finger Protein 41 (RNF41) which is also known to be involved in the trafficking of various transmembrane proteins. USP8 is a known substrate of RNF41 whereby RNF41 redistributes and ubiquitylates USP8, thus reducing USP8 levels. Balanced reciprocal cross-regulation between RNF41 and USP8 determines if receptors are sorted for lysosomal degradation or recycling, this way regulating basal cytokine receptor levels (De Ceuninck *et al.*, 2013). Recent cell-based and *in vivo* work has shown that the inhibition of USP8 activity or reduction in USP8 expression can selectively kill non-small cell lung cancer (NSCLC) cells. USP8 suppression leads to the downregulation of multiple oncogenic receptor tyrosine kinases (RTK); EGFR, ERBB2, ERBB3, and MET. Based on this work, USP8 has been proposed as a potential therapeutic target for both gefitinib-resistant and sensitive NSCLC cells (Byun *et al.*, 2013).

USP14 (+Proteasome-VS@Kd)

Mammalian proteasomes are associated with three DUBs: USP14, UCHL5 (UCH37) and RPN11 (POH1). UCHL5 and USP14 reside on the regulatory particle and remove ubiquitin from the substrate before substrate degradation whereas RPN11's activity is delayed until the proteasome is committed to degrading the substrate (Lee *et al.*, 2010). The DUB activity of USP14 is known to be activated by proteasomes (recombinant USP14 catalytic activity is undetectable in the absence of proteasome activation). DUB*profiler* version 5 now offers USP14 (+Proteasome-VS@Kd) on the enzyme screening panel where the 26S Proteasome [Ub-VS treated] is at a concentration that binds to half the receptor sites on USP14 at equilibrium (Kd). The 26S proteasome preparation for this assay was prepared using the same protocol as described in Wang *et al.* (2007) and used by Lee *et al.*, (2010). The 26S proteasome endogenous DUB activity was removed – before the preparation was used to activate the recombinant USP14 for use in the DUB*profiler* assay – through washing and treatment with ubiquitin–vinyl-sulphone (Ub–VS) which forms an adduct with the active site cysteine in DUBs of the thiol protease class (Lee *et al.*, 2010).

The treatment of cultured cells with IU1 – an inhibitor of USP14 – enhanced the degradation of proteasome substrates implicated in neurodegenerative disease thus inhibition of this enzyme has been proposed as a potential strategy to reduce the levels of aberrant proteins in cells under proteotoxic stress (Lee *et al.*, 2010).

In the DUB*profiler* assay rather than refer to 'minus enzyme' wells for the zero percent activity control reference point (as for all other DUB enzymes), in the case of test compounds selected for the 'USP14 (+Proteasome-VS@Kd)' assay the data defining the zero percent activity control reference point is taken as that derived from the 'Proteasome-VS control' reaction containing the same test compound at the same concentration (see 'Proteasome-VS control' for details).

Proteasome-VS control

Alongside USP14 (+Proteasome-VS@Kd), we include a 26S proteasome-VS control well (the same reaction mix as above minus the USP14 enzyme). The 26S proteasome-VS has a small amount of residual proteasome-associated DUB activity remaining; hence why the data from this condition is referenced as the negative control in the calculation and reporting of 'USP14 (+Proteasome-VS@Kd)' test compound data. The 'Proteasome-VS

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control' reaction is automatically selected where screening versus 'USP14 (+Proteasome-VS@Kd)' is selected (see above for details).

USP16

USP16 (Ubp-M) has recently been implicated with somatic stem-cell defects in Down's syndrome. Although a few candidate genes have been linked to the spectrum of disorders associated with Down's syndrome, generally it is unclear how trisomy of specific genes contributes to the condition. Adorno *et al.* (2013) implicate the deubiquitylating enzyme USP16 in an impaired ability of adult-tissue stem cells to self-renew. Downregulation of USP16, either by mutation of a single normal USP16 allele or by short interfering RNAs, largely rescues all of these defects. Furthermore, in human tissues overexpression of USP16 reduces the expansion of normal fibroblasts and postnatal neural progenitors, whereas downregulation of USP16 partially rescues the proliferation defects of Down's syndrome fibroblasts. Taken together, these results suggest that USP16 has an important role in antagonizing the self-renewal and/or senescence pathways in Down's syndrome and could serve as an attractive target to ameliorate some of the associated pathologies. USP16 is known to deubiquitylate the most abundant mammalian chromatin protein, histone H2A and can also be phosphorylated by cyclin-dependent kinase 1 (CDK1). Phosphorylation at serine 552 (S552P) is required for cell cycle progression but is not required for its deubiquitylating activity, substrate specificity, or regulation of gene expression (Xu *et al.*, 2013). USP16 contains a zinc-finger ubiquitin binding domain (Znf-UBP) and similar to USP5, the unique ubiquitin-recognition mode of USP16's Znf-UBP suggests it may function as a "sensor" of free ubiquitin in cells to achieve regulatory roles in many aspects of ubiquitin-dependent processes (Pai *et al.*, 2007).

OTUD5 (p177S)

OTUD5 (or DUBA) belongs to the ovarian tumour sub-family of DUBs. Phosphorylation of OTUD5 at a single residue, Ser177, is both necessary and sufficient to activate the enzyme. A network of interactions involving the phosphate and the C-terminal tail of ubiquitin cause OTUD5 to fold around its substrate, revealing why phosphorylation is essential for deubiquitylase activity. Phosphoactivation of OTUD5 represents an intriguing new mode of protease regulation and a clear link between two major cellular signal transduction systems: phosphorylation and ubiquitin modification (Huang *et al.*, 2012). OTUD5 has been shown to selectively cleave K63–linked polyubiquitin chains on tumour necrosis factor receptor–associated factor 3 (TRAF3), an E3 ubiquitin ligase that preferentially assembles K63–linked polyubiquitin chains. Removal of these K63 polyubiquitin chains from TRAF3 results in its dissociation from the downstream signalling complex containing TANK binding kinase 1 (TBK1) (Kayagaki *et al.*, 2007).

References:

Adorno M, Sikandar S, Mitra SS, Kuo A, Nicolis Di Robilant B, Haro-Acosta V, et al. (2013) Usp16 contributes to somatic stem-cell defects in Down's syndrome. *Nature*, **501**, 380-384.

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Lee BH, Lee MJ, Park S, Oh DC, Elsasser S, Chen PC, *et al.* (2010) Enhancement of proteasome activity by a small-molecule inhibitor of USP14. *Nature*, **467**, 179-184.

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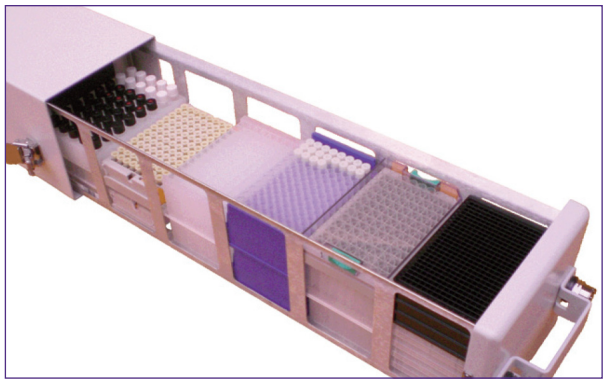
Wang X, Chen CF, Baker PR, Chen PL, Kaiser P and Huang L (2007) Mass spectrometric characterization of the affinity-purified human 26S proteasome complex. *Biochemistry*, **46**, 3553-3565.

Xu Y, Yang H, Joo HY, Yu JH, Smith ADt, Schneider D, *et al.* (2013) Ubp-M serine 552 phosphorylation by cyclin-dependent kinase 1 regulates cell cycle progression. *Cell Cycle*, **12**, 3219-3227.

NEW - DUB*profiler* Compound Storage System

Ubiquigent has implemented a StoragePod® system for DUB*profiler* compound management. The StoragePod® is a modular storage solution designed to prevent damaging moisture and oxygen uptake during the storage of compounds. This is particularly useful when storing compounds in DMSO.

The inert atmosphere inside the StoragePod® reduces the need for freeze-thaw cycles which can lead to sample precipitation and increases the risk of moisture uptake.



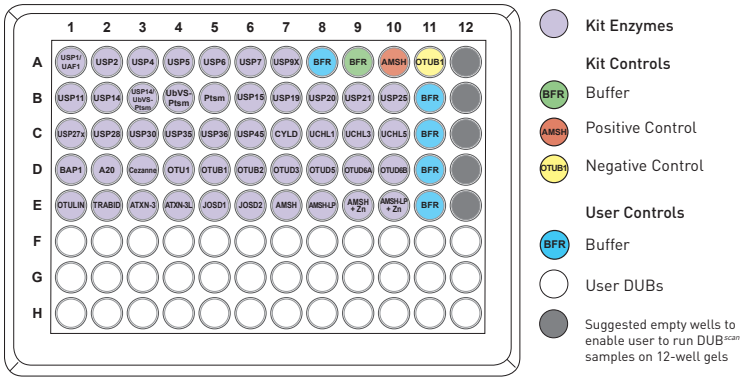
Ubiquigent's compound storage system is as follows:

- Your compounds will remain frozen (stored at -80˚C) until the day of profiling.
- On the day of profiling, your compounds will be thawed and will remain at room temperature in a StoragePod® when not being tested.
- We will discard of your compounds 6 months after the completion of your DUB*profiler* project.

Related Product: DUB*scan*™ Kit

The DUB*scan* kit has been flexibly designed for many potential valuable applications. One is the identification of DUB enzymes which catalyse the deubiquitylation of a substrate protein of interest.

The kit contains a DUB*scan* plate (a panel of DUBs arrayed across 47 wells of a 96 well plate) plus a control ubiquitylation reaction mix for performing both positive and negative control deubiquitylation reactions.



DUB*scan* Kit — Cat. # 67-0006-001

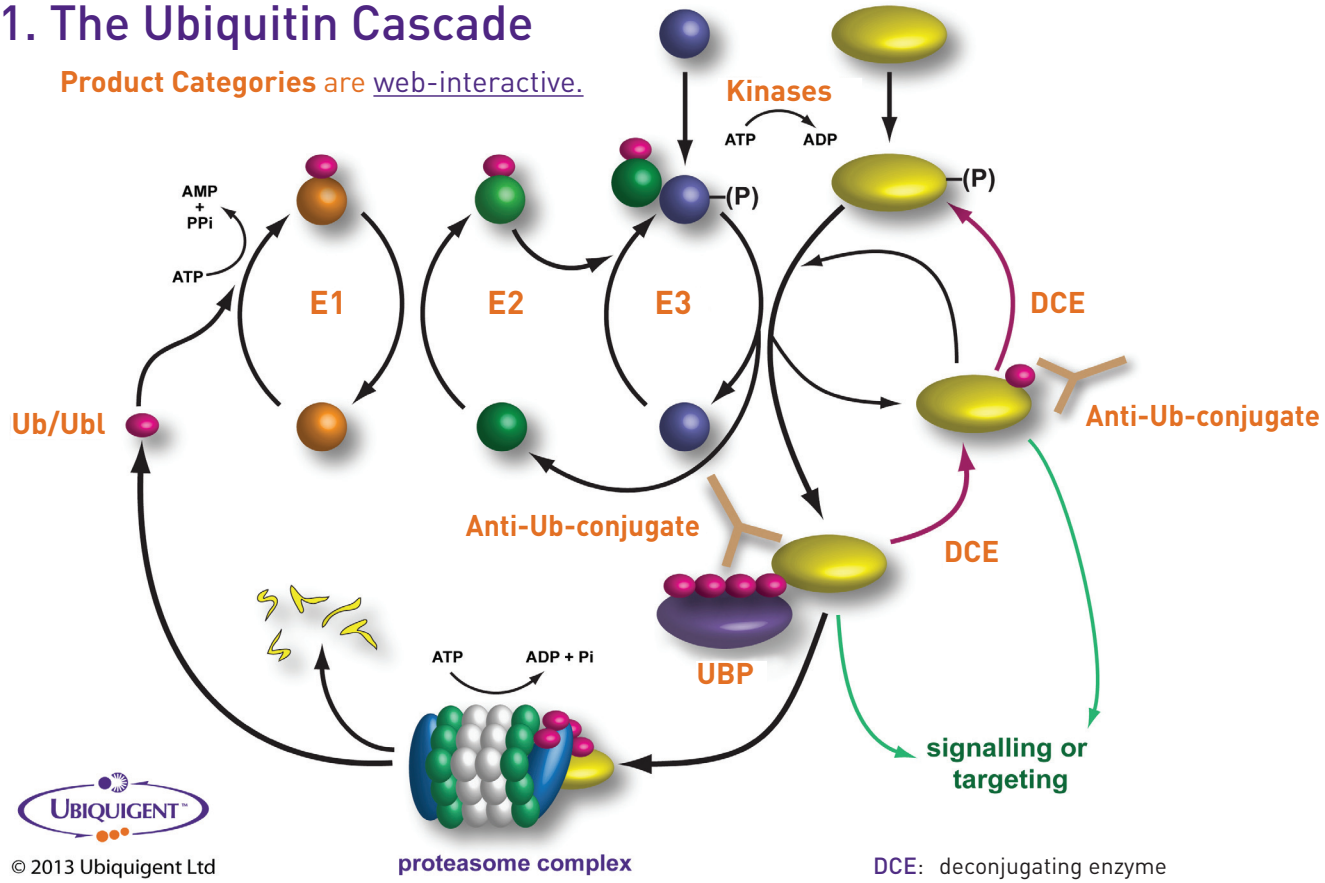
Why use the DUB*scan* kit?

- Examine the cleavage of *in vitro* ubiquitylated substrates generated using different E2/E3 combinations (refer to the **Ubiquigent E2*scan*™ Kit Version 2** for identifying E2s that 'couple' with your E3 of interest)
- Examine the cleavage of *in vivo* ubiquitylated substrates after capture from a cell lysate (refer to Ubiquigent **ubiquitin chain binding proteins** for capturing ubiquitylated proteins)
- Investigate DUB ubiquitin-ubiquitin linkage cleavage specificity (refer to Ubiquigent **di-ubiquitin and ubiquitin chains** for use as substrates)
- Examine the relative position of cleavage within ubiquitin chains (distal versus proximal)
- Explore mono and poly-deubiquitylation DUB specificity (refer to specific Ubiquigent **E2s** – such as Ube2W – for mono-ubiquitylating E2s)
- Explore potential DUB inhibitors and/or activators
- Identify novel DUB binding proteins
- Explore how DUBs may interact with and modify the activity of other ubiquitin system proteins such as E2s and *vice versa*

2 Ways to Find UBIQUIGENT Products Fast!

1. The Ubiquitin Cascade

Product Categories are web-interactive.



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DCE: deconjugating enzyme
Ub: ubiquitin
Ubl: ubiquitin-like protein

2. Drug Discovery Services and Reagent List

- **Comprehensive**
- **Downloadable**
- **Print-Friendly**
- **Catalogue #s link to website descriptions**

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