Deciphering the Ubiquitin CODE by chemical tools

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List of abbreviations

ABP	Activity-Based Probe
ADP	Adenosine Diphosphate
AffBP	Affinity-Based Probe
AMP	Adenosine Monophosphate
APF1	ATP-Dependent Proteolysis Factor 1
ARIH1	Ariadne Homolog 1
ARIH2	Ariadne Homolog 2
ATP	Adenosine Triphosphate
CHAPS	3-[(3-Cholamidopropyl)dimethylammonio]-1-propane-sulfonate
CHTOP	Chromatin Target of PRMT1
CNX	Calnexin
CuAAC	Copper(I)-catalyzed Azide-Alkyne Cycloaddition
CULLIN	Cullin Proteins
DCM	Dichloromethane
DIPEA	N,N-Diisopropylethylamine
DMSO	Dimethyl Sulfoxide
DNA	Deoxyribonucleic Acid
DTT	Dithiothreitol
DUB	Deubiquitinating Enzyme
ELISA	Enzyme-Linked Immunosorbent Assay
FI	Fluorescence Intensity
FP	Fluorescence Polarization
FPLC	Fast Protein Liquid Chromatography
FRET	Förster Resonance Energy Transfer

HBTU	2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium Hexafluorophosphate
HECT	Homologous to the E6-AP Carboxyl Terminus
HEK293T	Human Embryonic Kidney 293T Cells
HeLa	Human Cervical Carcinoma Cell Line
HERC	HECT and RLD Domain Containing E3 Ubiquitin Ligase
HOBT	1-Hydroxybenzotriazole
HOOBT	N-Hydroxy-1,2,3-Benzotriazole
HTS	High Throughput Screening
ISG15	Interferon-Stimulated Gene 15
MES	2-(N-Morpholino)ethanesulfonic Acid
MINDY	Motif-Interacting with Ubiquitin-Containing Novel DUB Family
MJDS	Machado-Joseph Disease Containing Protein
MS	Mass Spectrometry
NEBES	NEDD8 Binding Entities
NEDD4L	NEDD4-like E3 Ubiquitin Ligase
NEDD8	Neural Precursor Cell Expressed Developmentally Down-Regulated Protein 8
NEDP1	NEDD8-Processing Enzyme 1
NMP	N-Methyl-2-Pyrrolidone
NMR	Nuclear Magnetic Resonance
OTU	Sixteen ovarian tumor DUB family
PBS	Phosphate-Buffered Saline
PROTAC	Proteolysis Targeting Chimeras
PSMBD	Proteasomal Subunit Binding Domain
PSMC	Proteasome 26S Subunit, ATPase 6
PTM	Post-Translational Modification

RBR	RING Between RINGs
RCR	RING Cysteine Relay
RING	Really Interesting New Gene
RNF4	Ring Finger Protein 4
SDS	Sodium Dodecyl Sulfate
SEC	Size Exclusion Chromatography
SENP	SUMO/Sentrin Specific Proteases 1-7
SIM	SUMO Interaction Motif
SPPS	Solid-Phase Peptide Synthesis
SUBES	SUMO Binding Entities
SUMO	Small Ubiquitin-like Modifier
TCEP	Tris(2-carboxyethyl)phosphine
TEOTA	Triethyl 2,2',2''-((nitrilotris(methylene))tris(1H-1,2,3-triazole-4,1-diyl))triacetate
TRIS	Tris(hydroxymethyl)aminomethane
TUBES	Tandem Ubiquitin Binding Entities
Ub	Ubiquitin
UBA	Ubiquitin-Associated Domain
UBD	Ubiquitin Binding Domain
Ubl	Ubiquitin-like Domain
UBR5	Ubiquitin Protein Ligase E3 Component N-Recognin 5
UIM	Ubiquitin-Interacting Motif
UIML	Ubiquitin Interacting Motif Like
UPS	Ubiquitin-Proteasome System
USP	Ubiquitin-Specific Protease
XPC	Xeroderma Pigmentosum Group C
ZUFSP	Zinc Finger with UFM1-specific peptidase domain protein

List of publications

Pérez Berrocal, D. A., Thimmalapura M. Vishwanatha, Daniel Horn-Ghetko, J. Josephine Botsch, Laura A. Hehl, Sebastian Kostrhon, Mohit Misra, Ivan Đikić, Paul P. Geurink, Hans van Dam, Brenda A. Schulman & Monique P.C. Mulder1. A Pro-Fluorescent Ubiquitin-Based Probe to Monitor Cysteine-Based E3 Ligase. Angew Chem Int Ed Engl. 2023 Aug 7;62(32). doi: 10.1002/anie.202303319

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Curriculum Vitae

David Aureliano Pérez Berrocal, born on September 26, 1993, in Madrid, Spain, earned his Bachelor's degree in Chemistry in 2015 from the University Complutense of Madrid, Spain. He completed his final year in Wroclaw, Poland in the Porphyrin chemistry research group led by Prof. Dr. Lechosław Latos-Grażyński under the supervision of Dr. Milos Pawlicki, where he conducted hardcore organo-metallic chemistry to synthesize a new scaffold-type of phorphirins and investigated their paramagnetic properties.

In 2016, he obtained his Master's in Organic Chemistry (Medicinal Chemistry specialization) from the University Complutense of Madrid, Spain. During his master studies, he joined the Medicinal Chemistry research group led by Prof. Dr. Maria Luz Rodriguez, focusing on the endocannabinoid system and synthesizing cannabidiol derived chemical probes to identify its unknown molecular receptors for neurodegenerative disease research. After completion, he continued this work as a research assistant.

In 2018, he began his PhD under the Horizon ITN-Marie Curie UbiCODE consortium in the Chemical Biology Laboratory of Prof. Dr. Huib Ovaa under the supervision of Dr. Monique Mulder at Leiden University Medical Centrum (LUMC), The Netherlands, developing tools to study the Ubiquitin Proteasome System. In this multidisciplinary environment at the interface of chemistry and (medical) biology, chemical tools were used to unravel the complex biological language of the Ub CODE, where he focused on signaling mediated by the interactions of Ub-SUMO2 hybrid chains, as well as the development of E3 Ligase activity assays and small molecule modulators. In 2022, he visited the Molecular Machines Department led by Prof. Dr. Brenda Schulman at Max Planck Institute (MPI), Martinsried-Munich for his secondment. The primary findings of his research are described in this dissertation. At the end of 2022, he continued his research as a post-doctoral fellow under the public-private consortium EUbOPEN. He is now transitioning from academia to industry.

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