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Repurposing ubiquitination for innovative antibody conjugation

Hebieshy, A.F. el

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Curriculum Vitae

Angela el Hebieshy was born on the 21st of February 1989 in Hulst, the Netherlands. From a young age, she harbored a strong interest in biomedical sciences and biotechnology and in 2012, she obtained her Bachelor's degree in Clinical Pharmacy from the Suez Canal University in Ismailia, Egypt. Eager to pursue her research interests, she moved back to the Netherlands to study the Drug Discovery and Safety Master's program at the VU Amsterdam from 2012 to 2015, specializing in Molecular Pharmacology. During her Master's, Angela joined Huib Ovaa's research group for an internship, a decision that profoundly shaped her career. It was soon clear to her that this was the research group where she found the scientific freedom and encouragement to thrive as a scientist. And hence, following her internship she transitioned to a full-time role, initially as a technician for one year after which she started her PhD trajectory under his supervision. During her PhD, she developed Ubi-tagging, a modular site specific antibody conjugation technology that provides a new method for the development of antibody-based vaccines, antibody-based research and diagnostic tools, and multispecific antibody complexes. What started as a side project, quickly grew into multiple big projects with great potential. Filing the patent application for the Ubi-tagging technology, sparked her interest in entrepreneurship and that was the moment when she decided that the next step in her career will be towards the life sciences industry. Currently, she is working as a Project and Grant Manager at FFUND, a life sciences consultancy company, where she manages projects and portfolios of multiple grants and loans that run through research departments and innovative companies.

Publications

Journal articles

Site-directed multivalent conjugation of antibodies to ubiquitinated payloads

Angela F. el Hebieshy*, Zacharias Wijffes*, Camille M. Le Gall, Jim Middelburg, Kim E. de Roode, Felix L. Fennemann, Marjolein Sluijter, Thorbald van Hall, Douwe J. Dijkstra, Leendert A. Trouw, Floris J. van Dalen, Andrea Rodgers Furones, Johan M.S. van der Schoot, Ian Derksen, Hans de Haard, Bas van der Woning, Cami M.P. Talavera Ormeño, Bjorn R. van Doodewaerd, Carl G. Figdor, Gerbrand J. van der Heden van Noort, Paul W.H.I. Parren, Sandra Heskamp, Huib Ovaa, Martijn Verdoes, Ferenc A. Scheeren. Accepted for publication: Nature Biomedical Engineering.

Total Chemical Synthesis of a Functionalized GFP Nanobody.

Angela F. el Hebieshy*, Yara Huppelschoten*, Dharjath S. Hameed, Aysegul Sapmaz, Jens Buchardt, Thomas E. Nielsen, Huib Ovaa, Gerbrand J. van der Heden van Noort. ChemBioChem, vol. 23, no. 19, p. e202200304, Oct. 2022, doi: 10.1002/CBIC.202200304.

Thermal-exchange HLA-E multimers reveal specificity in HLA-E and NKG2A/CD94 complex interactions.

Paula Ruibal, Ian Derksen, Marjolein van Wolfswinkel, Linda Voogd, Kees L.M.C. Franken, Angela F. el Hebieshy, Thorbald van Hall, Tom A.W. Schoufour, Ruud H. Wijdeven, Tom H.M. Ottenhoff, Ferenc A. Scheeren, Simone A. Joosten. Immunology. 2023 Mar;168(3):526-537. doi:10.1111/imm.13591.

Malaria parasite evades mosquito immunity by glutaminy cyclase-mediated posttranslational protein modification.

Surendra Kumar Kolli, Alvaro Molina-Cruz, Tamasa Araki, Fiona J.A. Geurten, Jai Ramesar, Severine Chevalley-Maurel, Hans J. Kroeze, Sascha Bezemer, Clarize de Korne, Roxanne Withers, Nadia Raytselis, Angela F. el Hebieshy, Robbert Q. Kim, Matthew A. Child, Soichiro Kakuta, Hajime Hisaeda, Hirotaka Kobayashi, Takeshi Annoura, Paul J. Hensbergen, Blandine M. Franke-Fayard, Carolina Barillas-Mury, Ferenc A. Scheeren, Chris J. Janse. Proc Natl Acad Sci U S A. 2022 Aug 30;119(35):e2209729119. doi: 10.1073/pnas.2209729119. Epub 2022 Aug 22.

Temperature-based MHC class-I multimer peptide exchange for human HLA-A, B and C.

Cilia R. Pothast, Ian Derksen, Anneloes van der Plas-van Duijn, Angela F. el Hebieshy, Wesley Huisman, Kees L.M.C. Franken, Jacques Neefjes, Jolien J. Luimstra, Marieke Griffioen, Michel Kester, Maarten H. Vermeer, Mirjam H.M. Heemskerk, Ferenc A. Scheeren. bioRxiv 2024.12.23.630039; doi: https://doi.org/10.1101/2024.12.23.630039

Synthetic and semi-synthetic strategies to study ubiquitin signaling.

Gabriëlle B.A. van Tilburg, Angela F. el Hebieshy, and Huib Ovaa. Curr Opin Struct Biol, vol. 38, pp. 92–101, Jun. 2016, doi: 10.1016/J.SBI.2016.05.022.

Patents

Polypeptide conjugates.

Ferenc A. Scheeren, Huib Ovaa and Angela F. el Hebieshy. WO2020101498A1. 22 May, 2020.

Portfolio

PhD student:	AF el Hebieshy	F
Primary thesis advisor:	prof.dr. JJC Neefjes	
Other thesis advisor(s):	dr. FA Scheeren	
	dr. GJ van der Heden van Noort	
Research programme:	40801 Chemical Immunology	
Title of Thesis:	Repurposing ubiquitination for innovative antibody conjugation	

PhD training

	Year	Hours
Mandatory courses		
- Leiden University Onboarding Programme Inform & Connect (2 activities) (exempted)		5
- Responsible Research (2 activities) (exempted)		42
- Basic Methods and Reasoning in Biostatistics (exempted)		42
Generic/disciplinary courses		
- Confocal Microscopy training LUMC	2016	3
- Flowcytometry training LUMC	2017	3
- BioLegend/Excyte Flow Cytometry training	2019	15
- Biobusiness winter school	2021	24
- Presentation skills for PhDs	2018	16
- Time and project management (ICI)	2017	16
- Communication in Science (ICI)	2016	16
- Personal leadership (ICI)	2017	16
- Experimental Oncology (NKI)	2016	40
Attended lectures, LUMC presentations, participation in meetings		
- Literature meeting	2017	8
- Literature meeting	2018	8
- Literature meeting	2019	8

- CCB Meeting	2018	8
- CCB Meeting	2020	8
- CCB Meeting	2021	8
Congress attendance and poster or oral presentations		
- ICI PhD day	2017	8
- CHAINS	2018	24
- CHAINS	2021	16
- CHAINS	2022	16
- Next generation Antibodies and Protein analysis (Gent)	2017	16
Teaching activities		
Lecturing, lab assistance, student supervision		
- FOS Course student supervision	2017	40
- FOS Course student supervision	2018	40
- Supervision of Intern Ian Derksen	2019	200
TOTAL number of hours		646

Publications

Publications in peer reviewed journals (article, review, editorial, letter to editor)

	Year
- Synthetic and semi-synthetic strategies to study ubiquitin signaling; van Tilburg Gabrielle B. A., Elhebieshy Angela F., Ovaa Huib; 2016; Journal article	2016
- Malaria parasite evades mosquito immunity by glutaminyl cyclase-mediated posttranslational protein modification; Kolli, S.K.; Molina-Cruz, A.; Araki, et al.; 2022; Journal article	2022
- Thermal-exchange HLA-E multimers reveal specificity in HLA-E and NKG2A/CD94 complex interactions; Ruibal P, Derksen I, van Wolfswinkel M, et al.; 2022; Journal article	2022
- Total chemical synthesis of a functionalized GFP nanobody; Huppelschoten Y, Elhebieshy AF, Hameed DS, et al.; 2022; Journal article	2022
- Polypeptide Conjugates; 2020; Scheeren FA, Ovaa H and El Hebieshy AF.	2020

Acknowledgements

I am profoundly grateful to my late promotor, Huib Ovaa, whose support and guidance during the first half of my PhD trajectory have been pivotal in my pursuit of the work I am passionate about. His belief in my capabilities and his mentorship have significantly shaped my growth as a scientist and as a person, for which I am eternally thankful. I would also like to express my sincere appreciation to my promotor Jacques Neefjes, who graciously stepped in and provided stability and guidance following Huib's passing. I also wish to extend my thanks to my co-promotor Ferenc Scheeren, for his unwavering support and belief in my potential throughout my PhD. His presence and guidance at every step have been a source of strength and inspiration. I am equally thankful to Gerbrand van der Heden van Noort, for his readiness and efficiency in providing guidance and support when it was most needed, which has been invaluable and greatly appreciated. Additionally, I must acknowledge the crucial contributions of my collaborators, whose efforts have been fundamental to the success of this work and my colleagues for their unwavering support and for the fun and friendly working environment that greatly enriched my experience.

