

SPRINGER BRIEFS IN MOLECULAR SCIENCE  
PROTEIN FOLDING AND STRUCTURE

Vladimir N. Uversky

# Intrinsically Disordered Proteins

 Springer

# **SpringerBriefs in Molecular Science**

Protein Folding and Structure

**Series editor**

Cláudio M. Gomes, Oeiras, Portugal

## About the Series

Prepared by leading experts, the series contains diverse types of contributions, from snapshot volumes that allow fast entry to a general topic to those covering more specialized aspects in the field of protein folding and structure. In common, these *Briefs* aim at covering essential concepts, methodologies, and ideas in the context of contemporary research in protein science. Through these compact volumes, this series serves as a venue for publication between typical research papers, review articles and full books, and aims at a broad audience, from students to researchers in academia and industry.

## About the Editor



**Cláudio M. Gomes** joined the Gulbenkian Ph.D. program in Biology and Medicine (1994) and obtained his Ph.D. in Biochemistry (1999) from the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa. His research is focused on protein folding, misfolding and aggregation, mostly concerning molecular mechanisms in neurodegenerative and metabolic diseases. He is involved in extensive publishing and editorial activities, as an author in scientific journals, member of the Editorial boards of several scientific journals and editor of thematic journals issues and books.

More information about this series at <http://www.springer.com/series/11958>

Vladimir N. Uversky

# Intrinsically Disordered Proteins

 Springer

Vladimir N. Uversky  
Department of Molecular Medicine  
University of South Florida  
Tampa, FL  
USA

ISSN 2199-3157                      ISSN 2199-3165 (electronic)  
ISBN 978-3-319-08920-1          ISBN 978-3-319-08921-8 (eBook)  
DOI 10.1007/978-3-319-08921-8

Library of Congress Control Number: 2014945349

Springer Cham Heidelberg New York Dordrecht London

© The Author(s) 2014

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law. The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media ([www.springer.com](http://www.springer.com))

# Foreword

The perspective of changing established paradigms is a fascinating aspect of the scientific endeavor. In structural biology, a long-standing paradigm has been the one that protein structure determines function and its reciprocal, that protein function is determined by structure. This view roots on the pioneering reports of protein structures determined using X-ray crystallography already over half a century ago, and has gained momentum with a wealth of protein three-dimensional structures which have been experimentally determined ever since. Undoubtedly, a well-folded protein structure is the hallmark attribute of protein function for many types of proteins, notably those adopting a globular fold. Nevertheless, today we also know that many proteins contain functional disordered segments or are wholly disordered, lacking well-defined three-dimensional structures, but are yet able to adopt an ensemble of functional conformations. Such proteins that challenge the structure-function paradigm are coined as intrinsically disordered, and are nowadays broadly accepted as important players in cellular functions. In this volume, the leading expert Vladimir N. Uversky provides us with an excellent overview on different aspects of this important area in protein structural biology. Through a direct, yet comprehensive presentation of the fundamental concepts, characteristics, and functions of intrinsically disordered proteins, along with valuable personal notes and historical insights, Uversky presents us with state-of-the-art knowledge and delivers a view of promising roles of intrinsically disordered proteins in biomedicine. As the Editor, I can hardly imagine a better inaugural volume for the *SpringerBriefs* series on *Protein Folding and Structure* than a volume dealing with *Intrinsically Disordered Proteins*, a paradoxical and debatable concept in the past of structural biology, but certainly one of the most promising future areas of protein research.

Oeiras, May 2014

Cláudio M. Gomes

# Acknowledgements

Over the years, I collaborated with more than 700 colleagues from more than 100 universities in more than 20 countries. This work would be impossible without these numerous collaborators whose enthusiasm and help drove the studies on intrinsically disordered proteins for many years. In no particular order the list of people contributed to this project at its different stages includes: Eugene Permyakov, Joel Gillespie, Vyacheslav Abramov, Anthony Fink, Larissa Munishkina, Pierre Souillac, Sebastian Doniach, Ian Millett, Daniel Denning, Kevin Lee, Alexander Sigalov, Michael Rexach, Sergei Permyakov, Keith Oberg, Stefan Winter, Jie Li, Oxana Galzitskaya, Leonhard Kittler, Gunter Lober, Olga Tcherkasskaya, Seung-Jae Lee, Min Zhu, Amy Manning-Bog, Alison McCormack, Donato Di Monte, Kiowa Bower, I-Hsuan Liu, Gregory Cole, John Goers, Ghiam Yamin, Atta Ahmad, Charles Glaser, Elisa Cooper, Jeffrey Cohlberg, Mark Hokenson, Sudha Rajamani, Joseph Zbilut, Alessandro Giuliani, Alfredo Colosimo, Julie Mitchell, Mauro Colafranceschi, Norbert Marwan, Charles Webber, Jr., Christopher Oldfield, Yugong Cheng, Marc Cortese, Celeste Brown, Mikhail Karymov, Yuri Lyubchenko, Pedro Romero, Lilia Iakoucheva, Zoran Obradovic, Véronique Receveur-Bréchet, Jean-Marie Bourhis, Bruno Canard, Sonia Longhi, Chad McAllister, Yoshiko Kawano, Alexander Lushnikov, Andrew Mikheikin, Andrey Vartapetyan, Predrag Radivojac, Slobodan Vucetic, Timothy R. O'Connor, Jag Bhalla, Geoffrey Storch, Caitlin MacCarthy, Maureen Harrington, Tanguy LeGall, Patrizia Polverino de Laureto, Laura Tosatto, Erica Frare, Oriano Marin, Angelo Fontana, Megan Sickmeier, Justin Hamilton, Vladimir Vacic, Agnes Tantos, Beata Szabo, Peter Tompa, Jake Chen, King Pan Ng, Gary Potikyan, Rupert Savene, Christopher Denny, Vinay Singh, Yue Zhou, Joseph Marsh, Julie Forman-Kay, Jingwen Liu, Zongchao Jia, Millie Georgiadis, Amrita Mohan, Ann Roman, Jiangang Liu, Narayanan Perumal, Eric Su, Fei Ji, Niels Klitgord, Michael Cusick, Marc Vidal, Chad Haynes, Saima Zaidi, Ya Yin Fang, Jessica Chen, Igor Lednev, Bin Xue, Leo Breydo, Madan Babu, Richard Kriwacki, Ming Xu, Vladimir Ermolenkov, Vitali Sikirzhyski, Natalya Topilina, Gaius Takor, Seiichiro Higashiya, John Welch, Konstantin Turoverov, Irina Kuznetsova, Dickran Aivazian, Lawrence Stern, Hongbo Xie, Liwei Li, Samy Meroueh, Garret Anderson, Rafael Lujan,

Arthur Semenov, Marco Pravetoni, Joseph Song, Ching-Kang Chen, Kevin Wickman, Kirill Martemyanov, Ekaterina Posokhova, Alexey Uversky, William Sullivan, Ágnes Tóth-Petróczy, Bálint Mészáros, István Simon, Monika Fuxreiter, Jeffrey Hansen, Francisco Asturias, Yuichiro Takagi, Oleg Paliy, Shawn Gargac, Alfredo De Biasio, Corrado Guarnaccia, Matija Popovic, Alessandro Pintar, Sándor Pongor, Mona Rahman, Kim Munro, Steven Smith, Ivan Pacheco, John MacLeod, Anush Bakunts, Alexander Denesyuk, Ekaterina Knyazeva, Ramil Ismailov, Gerard Goh, Kimmo Rantalainen, Perttu Permi, Nisse Kalkkinen, Kristiina Mäkinen, Siyuan Ren, Zhengjun Chen, Fabien Durand, Adilia Dagkessamanskaia, Helene Martin-Yken, Marc Graille, Herman Van Tilbeurgh, Matteo Binda, Frédéric Lopez, Karim El Azzouzi, Jean-Marie Francois, Andrew Campen, Ryan Williams, Joel Sussman, Israel Silman, Dong-Pyo Hong, Nobuhiko Tokuriki, Igor Berezovsky, Dan Tawfik, Eugénie Hébrard, Yannick Bessin, Thierry Michon, François Delalande, Alain Van Dorsselaer, Jocelyne Walter, Nathalie Declerk, Denis Fargette, Wenbo Zhou, Carlo Santambrogio, Stefania Brocca, Rita Grandori, Mária Šamaliková, Marina Lotti, Marco Vanoni, Lilia Alberghina, Lorenzo Testa, Annalisa D'Urzo, Johnny Habchi, Uros Midic, Bo He, Kejun Wang, Yunlong Liu, Xiaoyun Meng, David Eliezer, Victor Kutyshenko, Dmitry Prokhorov, Maria Timchenko, Yuri Kudrevatykh, Liubov' Gushchina, Vladimir Khristoforov, Vladimir Filimonov, Agyakojo Frimpong, Rinat Abzalimov, Igor Kaltashov, Roland Dunbrack, Robert Williams, Xiaolin Sun, William Jones, Erik Rikkerink, David Greenwood, Matthew Templeton, David Libich, Tony McGhie, Minsoo Yoon, Wei Cui, Christopher Kirk, Dawn Harvey, Patrick Edwards, Steven Pascal, Christopher Kirk, Thérèse Considine, David Sheerin, Jasna Rakonjac, Wei-Lun Hsu, Jun-Ho Lee, Hua Lu, Rajarshi Ghosh, Tatiana Nikitina, Rachel Horowitz-Scherer, Lila Gierasch, Kristopher Hite, Jeffrey Hansen, Christopher Woodcock, Perna Malaney, Ravi Pathak, Vrushank Davé, Jaymin Kathiriya, Eric Clayman, Aaron Satner, Julian Jorda, Andrey Kajava, Hayriye Erkizan, Jeffrey Toretzky, Justin Yamada, Joshua Phillips, Samir Patel, Gabriel Goldfien, Alison Calestagne-Morelli, Hans Huang, Ryan Reza, Justin Acheson, Viswanathan Krishnan, Shawn Newsam, Ajay Gopinathan, Edmond Lau, Michael Colvin, Olof Einarsdottir, Blanca Silva, Stacy Dixon, Micah Bhatti, Natalia Moroz, Stefanie Novak, Ricardo Azevedo, Mert Colpan, Carol Gregorio, Alla Kostyukova, Samar Shah, Yulia Gritsyna, Sarah Hitchcock-DeGregori, Mark Rochman, Leila Taher, Toshihiro Kurahashi, Srujana Cherukuri, David Landsman, Ivan Ovcharenko, Michael Bustin, Marcin Mizianty, Tuo Zhang, Yaoqi Zhou, Zhenling Peng, Fatemeh Miri Disfani, Lukasz Kurgan, Xiao Fan, Patrick Dolan, Douglas LaCount, Daniel Soeria-Atmadja, Mats Gustafsson, Ulf Hammerling, Franck Peysselon, Sylvie Ricard-Blum, Barbara Zambelli, Nunilo Cremades, Paolo Neyroz, Paola Turano, Stefano Ciurli, Fernanda Lopes, Olena Dobrovolska, Rafael Guerra, Valquiria Broll, Célia Carlini, Fei Huang, Colin Burns, Tuo Zhang, Eshel Faraggi, Bogdan Melnik, Tatiana Povarnitsyna, Anatoly Glukhov, Tatyana Melnik, Sandy Westerheide, Rachel Raynes, Chase Powell, Kuiran Xu, Ya-Yue Van, Maria Noutsou, Madelon Maurice,