

## Young Career Focus: Dr. Norman Metanis (Hebrew University of Jerusalem, Israel)

**Background and Purpose.** SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Norman Metanis (Hebrew University of Jerusalem, Israel).

### Biographical Sketch



Dr. N. Metanis

**Norman Metanis** earned his B.A. degree in Chemistry in 2000 (*Cum Laude*) from the Technion – Israel Institute of Technology, Haifa (Israel). He then moved to The Scripps Research Institute (TSRI), La Jolla (USA) as a visiting student and spent one year in the laboratories of Professors Ehud Keinan and Philip Dawson. Upon returning to the Technion, he completed his M.Sc. degree in 2004 (*Cum Laude*).

Then he moved back to TSRI where he again worked with Professors Ehud Keinan and Philip Dawson on a joint program between the Technion and TSRI. Upon the completion of his Ph.D. in 2008, Dr. Metanis joined the group of Professor Donald Hilvert at ETH Zurich (Switzerland) until 2013. Then he moved to the Institute of Chemistry at the Hebrew University of Jerusalem (Israel) as a Senior Lecturer (Assistant Professor). Among the awards that Dr. Metanis has received in the last five years are the Ma'of Award for Outstanding Arab Assistant Professor (2013), the Thieme Chemistry Journals Award (2017), and he was selected as outstanding lecturer for "Organic Chemistry for Medical Students" (2017).

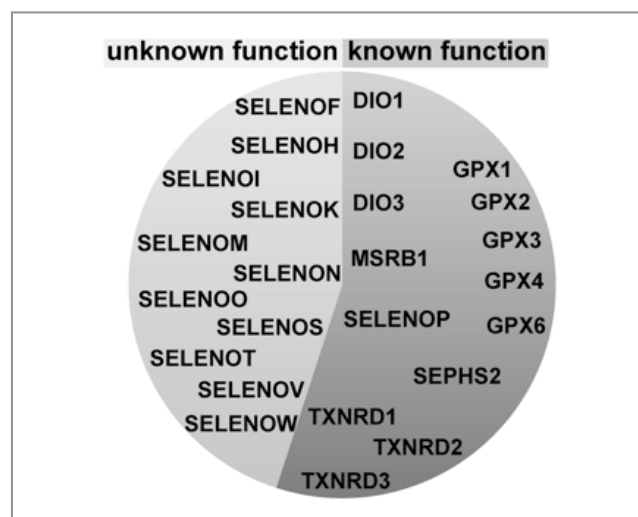
### INTERVIEW

**SYNFORM** What is the focus of your current research activity?

**Dr. N. Metanis** My research group is involved in multiple projects at the interface of chemistry and biology. Generally, we study the chemistry of proteins: protein folding, protein design, structural–activity relationships, posttranslational modifications, and therapeutic proteins. In particular, we focus on human selenoproteins,<sup>1</sup> a group of 25 proteins,<sup>2</sup> roughly half of which are still poorly characterized (Figure 1).

**SYNFORM** When did you get interested in synthesis?

**Dr. N. Metanis** I got interested in synthesis in my first year as an undergraduate when I attended organic chemistry cour-



**Figure 1** The human selenoproteins (roughly half of them still functionally uncharacterized or poorly studied)

ses at the Technion – Israel Institute of Technology. I started reading papers involving synthesis in the library of the chemistry department. I remember the pile of journals: *Tetrahedron*, *J. Am. Chem. Soc.* and *Angew. Chem.* among others, in hard copies, not electronically available at that time.

**SYNFORM** What do you think about the modern role and prospects of organic synthesis?

**Dr. N. Metanis** Organic synthesis keeps changing; it is hard to keep up with the new methodologies being developed by leading scientists. In addition, many young scientists play a role in these developments and are making leading discoveries in this field. New strong bond activation and functionalization methods will certainly have a significant impact on natural product synthesis, drug development, and other synthetic goals. Another field that is being pursued and developed in recent years is the application of chemoselective modifications to macromolecules such as nucleic acids and proteins. These modifications open new horizons in the field of chemical biology.

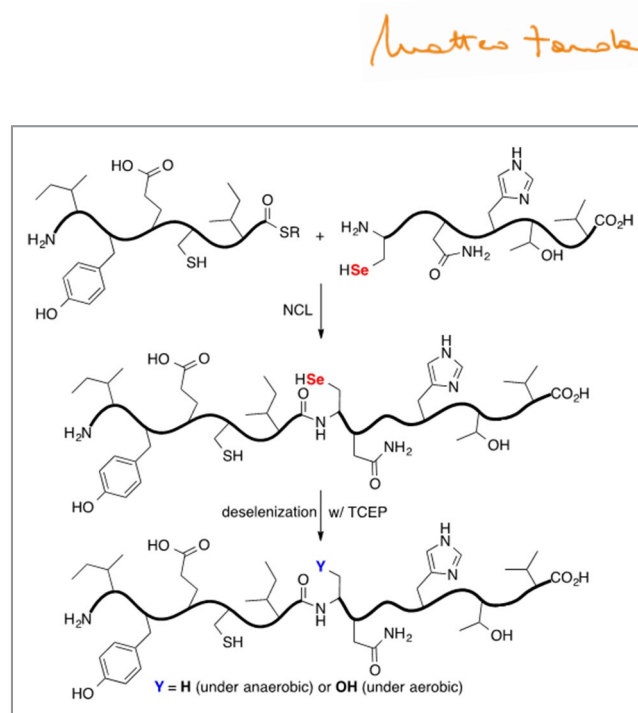
**SYNFORM** Your research group is active in the areas of protein and peptide chemistry. Could you tell us more about your research and its aims?

**Dr. N. Metanis** Indeed, my research group is active in the chemistry of peptides and proteins, from the development of new synthetic methodologies and chemoselective reactions applied to proteins, to the manipulation of protein structure in order to shed light on its function at the molecular level. Our current focus has been on elucidating the function of human selenoproteins (Figure 1). Generally, these are poorly studied proteins, since it is quite challenging to prepare them in sufficient quantities using biological methods. Along these lines, we recently succeeded in obtaining two human selenoproteins,<sup>3</sup> SELENOM and SELENOW through chemical protein synthesis. This poorly studied family of proteins is now within reach and these syntheses should allow us to study them in detail in the future.

**SYNFORM** What is your most important scientific achievement to date and why?

**Dr. N. Metanis** My hope is that my most important scientific achievement is yet to come. Nonetheless, I have made some important contributions in the fields of protein folding and chemical protein synthesis. Specifically, through substitution of cysteine with selenocysteine (just a single atom change:

sulfur to selenium), we found that it is possible to steer folding in a predictive and more productive path that avoids the predominant formation of trapped intermediates that normally appear during folding of the wildtype protein.<sup>4–7</sup> Furthermore, during our early work on selenoproteins, we found, by serendipity, that selenocysteine can be converted selectively into alanine (referred to as deselenization) in the presence of unprotected cysteine residues using a common reductant [tris(2-carboxyethyl phosphine), TCEP].<sup>8</sup> We have developed this reaction as a way to expand the native chemical ligation (NCL), which is one of the most applied reactions in chemical protein synthesis, but was originally limited to ligations at cysteine, to ligation sites of alanine and serine (Figure 2),<sup>9,10</sup> both being among the most common residues in proteins.



**Figure 2** Native chemical ligation at selenocysteine followed by deselenization to provide Ala or Ser (depending on the conditions)

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