

**P.I. BIOGRAPHICAL SKETCH:** Provide the following information for the Principal Investigator. Do not exceed two pages.

### BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

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NAME Ning Wang		POSITION TITLE Postdoctoral Researcher	
eRA COMMONS USER NAME			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Zhongshan University, Guangzhou, P.R.China	B.Sc.	1994	Microbiology
Zhongshan University, Guangzhou, P.R.China	M.Sc.	1998	Molecular biology
University of Massachusetts Amherst, MA	Ph.D.	2007	Biochemistry and molecular biology

#### A. Ph. D. RESEARCH SUMMARY

##### Cotranslational and translocational events assist in the fidelity of glycoprotein maturation in the cell

The earliest steps of nascent protein folding are critical to its overall folding efficiency. Folding events start as soon as the protein is translocated into the endoplasmic reticulum lumen, where the co-translational machinery ensures the fidelity of protein folding by coupling molecular chaperones, foldases and folding sensors. We seek to investigate the co-translational maturation events of disease-related glycoproteins containing different membrane topology to determine the generality and substrate specificity of this process, to hopefully provide new insight of therapeutic methods by targeting protein maturation at early stages. A variety of cell biological, biochemical, and molecular biological approaches using cell-free assays, isolated organelles and live cells have been applied in this study. Our published work on the co-translational maturation of a type I membrane protein human tyrosinase has shown that Hsp70 family member BiP handed off tyrosinase to the lectin chaperones calnexin/calreticulin as glycans were added. The albino mutation of tyrosinase (C71R) diverges from the wild type maturation pathway co-translationally through its recognition by the oxidoreductase ERp57. Our current work on a type II membrane protein *influenza* neuraminidase (NA) subtype N9 has shown that calnexin co-translationally interacted with NA prior to calreticulin. This sequential manner was found to be a common feature of the ER assembly line determined by the membrane localization and soluble characteristics of calnexin/calreticulin, respectively. These interactions were required for the proper maturation of NA as NA aggregated if calnexin/calreticulin interaction was abolished by glycosylation inhibition or removal of specific glycans. Surprisingly, a subset of NA can form intermolecular disulfides co-translationally supporting NA homodimerization. NA co-translational dimerization also occurs for a NA mutant lacking the critical large loop disulfide bonds, indicating that the dimerization of the stem domain does not require proper folding of the top globular domain of NA. This represents an exception to the general rule that protein oligomerization happens after the folding of individual domains. Future work on a variety of other substrates will help illuminate a global pathway of glycoprotein co-translational maturation.

#### B. Positions and Honors

Professional Positions:

- 1998-2001 Master's student, Department of Molecular Biology, Key Laboratory of Gene Engineering of the Ministry of Education, State Key Laboratory for Biocontrol, Zhongshan University, Guangzhou, P.R. China
- 2001-2007 Ph.D student, Department of Biochemistry and Molecular biology, University of Massachusetts Amherst, MA
- 2007-present Postdoctoral researcher, Department of Biochemistry, Northwestern University Evanston, IL

Awards:

- 2008: Career support grant recipient, Northwestern University
- 2004: Travel Grant recipient, University of Massachusetts at Amherst
- 2001: Graduate student with highest honor, Excellence in Graduate study of Zhongshan University
- 2000: Research patent: Special nucleotide acid sequences and method of determining *Cordyceps sinensis*, patent number: 00114160.0
- 1999: Antai excellent graduate student award
- 1998 Admission to the graduate school with no mandatory tests required  
Excellence in undergraduate study of Zhongshan University
- 1997: Dubang excellent undergraduate student award

1995: Excellent undergraduate student scholarship

Presentations:

Oral Presentation

2000: Presentation at the 4<sup>th</sup> Asian Herpetological Conference, Chengdu, P.R. China,  
Presentation title: Molecular phylogeny of relic *Ranodon sibiricus* and its related taxa

Poster presentation

2008: Poster presentation at Cold Spring Harbor laboratory Molecular chaperones and stress responses conference  
Poster title: Study of compartmentalized protein misfolding/aggregation in *C.elegans* models of Alzheimer's disease

2004: Poster presentation at FASEB summer conference (Federation of American Societies for Experimental Biology), Saxtons River, VT  
Poster title: Co-translational folding of tyrosinase in semi-permeabilized melanocytes

2003-2006: Poster presentation at annual Molecular and Cellular Biology program retreat

2000: Poster presentation at the 4<sup>th</sup> Asian Herpetological Conference, Chengdu, P.R. China,  
Poster title: Molecular phylogeny of relic *Ranodon sibiricus* and its related taxa

1999: Abstract submission at the 10<sup>th</sup> International Congress on genes, gene families, and isozymes  
Abstract title: Molecular characteristics and evolutionary biology of relic *Ranodon sinbiricus* (amphibia)

### C. Publications

1. Wang N, Glidden EJ, Murphy SR, Pearse BR, and Hebert DN. The cotranslational maturation program for the type II membrane glycoprotein influenza neuraminidase. (J. Biol. Chem. 2008 Oct 10. [Epub ahead of print])
2. Bradley RP, Luke G, Wang N and Hebert DN. (2008) The ER glucosyltransferase post-translationally reglucosylates glycans on slow folding or non-native domains. J. Cell. Bio. 181(2):309-20.
3. Wang N, Hebert DN. (2006) Tyrosinase maturation through the mammalian secretory pathway: bringing color to life. Pigment Cell Res. 19(1):3-18. Review.
4. Wang N, Daniels R and Hebert DN. (2005) The cotranslational maturation of the type I membrane glycoprotein tyrosinase: the heat shock protein 70 system hands off to the lectin-based chaperone system. Mol Biol Cell. 16(8):3740-52.
5. Francis E, Wang N, Parag H, Halaban R, Hebert DN. (2003) Tyrosinase maturation and oligomerization in the endoplasmic reticulum require a melanocyte-specific factor. J Biol Chem. 278(28):25607-17.
6. Chen YQ, Shao P, Wang N, Zhou H, Qu LH, Medlin LK. (2003) Molecular identification of blooming-forming species *Phaeocystis globosa* (Prymnesiophyta) and its dispersal based on rDNA ITS sequence analysis. Acta Oceanologica Sinica. 22(2): 243-253.
7. Chen YQ, Wang N, Zhang P, Zhou H, Qu LH. (2002) Molecular evidence identifies bloom-forming *Phaeocystis* (Prymnesiophyta) from coastal waters of southeast China as *Phaeocystis globosa*. Biochemical Systematics and Ecology. 30:15-22.
8. Chen YQ, Wang N, Zhou H, Qu LH, Yang LF, Lv HH and Qi YZ. (2002) Molecular identification and origin analysis on "red-tide" related *Phaeocystis* causative species. Acta Oceanologica Sinica. (24) 6:99-103.
9. Chen YQ, Wang N, Zhou H, Qu LH. (2002) Differentiation of medicinal *Cordyceps* species by rDNA ITS sequence analysis. Planta Med. (68): 635-639.
10. Chen YQ, Wang N, Qu LH, Li T and Zhang W. (2001) Determination of the anamorph of *Cordyceps sinensis* inferred from the analysis of the ribosomal DNA internal transcribed spacers and 5.8S rDNA. Biochem Syst Ecol. Jun; 29(6):597-607.
11. Wang N, Chen YQ, Qu LH, Lv HH, Qi YZ. (2000) Analysis of 18SrRNA Gene from a "red-tide" related *phaeocystis* species in south china sea. Acta Scientiarum Naturalium Universitatis Sunytseni. 39(1):127-128.
12. Wang N, Chen YQ, Zhang WM, Li TH and Qu LH. (2000) Molecular Evidences Indicating Multiple Origins in the Entomogenous *Cordyceps*. ACTA SCIENTIARUM NATURALIUM UNIVERSITATIS SUNYATSENI. 39(4):70-73.
13. Qu LH, Wang XL, Chen YQ, Wang N and Zhou H. (1999) Molecular Characteristics and Evolutionary Biology of Relic *Ranodon sibiricus* (Amphibia)( I ). Acta Scientiarum Naturalium Universitatis Sunytseni. 38(1):12-15.
14. Zhao J, Wang N, Chen YQ, Li TH, Qu LH. (1999) Molecular Identification for the Asexual Stage of *Cordyceps sinensis*. Acta Scientiarum Naturalium Universitatis Sunytseni.38(1):121-123.