

Xiaohu Huang

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EDUCATION AND TRAINING

- 09/2004-07/2008 **B.S.** in Biology
College of Life Sciences, Lanzhou University
- 09/2008-07/2013 **Ph.D.** in Biophysics
Institute of Molecular Medicine, Peking University
- 11/2013-Present Postdoctoral visiting fellow
National Institute of Child Health and Human Development (NICHD), NIH

RESEARCH EXPERIENCE

- 09/2008-07/2013 Ph.D. student, Institute of Molecular Medicine, Peking University
Supervisor: Heping (Peace) Cheng, Professor and Ming Zheng, Professor

Research Interests and Accomplishments:

1. Mitochondrial dynamics in adult cardiomyocyte

The most important finding of my study is the whole population of cardiac mitochondria forms a dynamically continuous network in adult cardiomyocyte, although they ostensibly look like separated, static and inert individuals. By using mitochondria-targeted photoactivatable green fluorescent protein (mtPAGFP) combined with confocal imaging, I identified two novel forms of inter-mitochondrial communication, termed mitochondrial “kissing” and “nanotunneling”, which are attributable to the cardiac mitochondrial network. EM microscopy further revealed mitochondrial kissing junctions and nanotubes, providing the structural basis of mitochondrial kissing and nanotunneling. These findings may shed new light on molecular mechanisms underlying cardiac mitochondrial communication, and possible roles in cardiac hypertrophy.

Reference:

Huang X, Sun L, Ji S, Zhao T, Zhang W, Xu J, Zhang J, Wang Y, Wang X, Franzini-Armstrong C, Zheng M, Cheng H. Kissing and nanotunneling mediate intermitochondrial communication in the heart. *Proc Natl Acad Sci U S A*. 2013;110(8):2846-51.

2. Role of mitochondrial fusion protein mitofusin 2 (MFN2) in heart

We found that specific deletion of MFN2 in cardiomyocytes caused extensive accumulation of autophagosomes by disturbing the fusion of autophagosomes with lysosomes, a critical step in autophagic degradation. Knockdown of MFN2 by shRNA prevented, whereas re-expression of MFN2 restored, the autophagosome-lysosome fusion in neonatal cardiomyocytes. Hearts from cardiac-specific MFN2 knock-out mice had abnormal mitochondrial and cellular metabolism and were vulnerable to ischemia-reperfusion challenge. Our study defined a novel and essential role

of MFN2 in the cardiac autophagic process by mediating the maturation of autophagy at the phase of autophagosome-lysosome fusion through interacting with RAB7.

Reference:

Zhao T, **Huang X**, Han L, Wang X, Cheng H, Zhao Y, Chen Q, Chen J, Cheng H, Xiao R, Zheng M. Central role of mitofusin 2 in autophagosome-lysosome fusion in cardiomyocytes. *J Biol Chem*. 2012;287(28):23615-25.

11/2013-Present Postdoctoral research
Molecular Medicine Program (MMP)
National Institute of Child Health and Human Development (NICHD), NIH
Supervisor: Tracey A Rouault, senior investigator

Research Interests and Accomplishments:

Role of LYRM7 in mediating maturation of mitochondrial cytochrome bc1 complex

Using biochemical methods, I found LYRM7 mediates Fe-S cluster transfer from iron-sulfur cluster assembly complex to its recipient protein UQCRFS1, a Fe-S containing subunit in mitochondrial cytochrome bc1 complex (CIII), by tethering iron-sulfur cluster assembly complex and Rieske protein UQCRFS1 together. Importantly, we also revealed that iron-sulfur cluster is transferred to UQCRFS1 in the mitochondrial matrix followed by insertion into CIII, but not in the mitochondrial intermembrane space after insertion, which has been under controversy and lack of evidence for decades. Now we are chasing how LYRM7 mediates the specific delivery of iron-sulfur cluster using mutation and truncated constructs of LYRM7 and UQCRFS1, which will provide the molecular mechanisms for pathogenesis of a mitochondrial encephalopathy in human which is as a result of the mutation of LYRM7.

Reference:

Huang X, Maio N, Zhang D, Rouault TA. Assembly factor LYRM7 mediates maturation of ubiquinone-cytochrome c reductase by delivering iron sulfur cluster to Rieske protein. In preparation.

TECHNICAL SKILLS

1. Microscopy and imaging:

Intravital imaging (*in vivo*); whole heart imaging (*ex vivo*); five years experiences in confocal and two-photon microscopy including photoactivation, photobleaching, FRAP and 3D construction. Experience in electron microscopy.

2. Molecular biology:

Molecular cloning; point mutation; DNA and RNA purification; quantitative RT-PCR; RNA interference; construction, amplification and purification of adenovirus.

3. Cell biology:

Cell culture and transfection; isolation and culture of cardiac myocytes; mitochondrial isolation and functional assays.

4. Biochemistry:

Protein expression and purification; western blotting; co-immunoprecipitation; immunofluorescence staining, immunocytochemistry.

5. Management of transgenic mice, and functional measurement of heart: echocardiography.

6. Computer skills:

Bioinformatics (such as sequence alignment and homology analysis, protein structure analysis, posttranslational modification analysis using database); IDL-based image processing; Image-J.

PUBLICATIONS

1. **Huang X**, Maio N, Zhang DL, Rouault TA. Assembly factor LYRM7 mediates maturation of ubiquinone-cytochrome c reductase by delivering iron sulfur cluster to Rieske protein. In preparation.
2. Lang H, Li Q, Yu H, Li P, Lu Z, Xiong S, Yang T, Zhao Y, **Huang X**, Gao P, Zhang H, Shang Q, Liu D, Zhu Z. Activation of TRPV1 attenuates high salt-induced cardiac hypertrophy through improvement of mitochondrial function. *Br J Pharmacol*. 2014 Oct 23. doi: 10.1111
3. Yue W, Chen Z, Liu H, Yan C, Chen M, Feng D, Yan C, Wu H, Du L, Wang Y, Liu J, **Huang X**, Xia L, Liu L, Wang X, Jin H, Wang J, Song Z, Hao X, Chen Q. A small natural molecule promotes mitochondrial fusion through inhibition of the deubiquitinase USP30. *Cell Res*. 2014;24(4):482-96.
4. **Huang X**, Sun L, Ji S, Zhao T, Zhang W, Xu J, Zhang J, Wang Y, Wang X, Franzini-Armstrong C, Zheng M, Cheng H. Kissing and nanotunneling mediate intermitochondrial communication in the heart. *Proc Natl Acad Sci U S A*. 2013;110(8):2846-51.
5. Zhao T, **Huang X**, Han L, Wang X, Cheng H, Zhao Y, Chen Q, Chen J, Cheng H, Xiao R, Zheng M. Central role of mitofusin 2 in autophagosome-lysosome fusion in cardiomyocytes. *J Biol Chem*. 2012;287(28):23615-25.

ABSTRACTS

1. **Xiaohu Huang**, Ting Zhao, Wanrui Zhang, Jiejia Xu, Shuangxi Ji, Xianhua Wang, Heping Cheng, Ming Zheng. Dynamically continuous network of mitochondria in adult rat cardiomyocyte. *Chinese Journal of Pathophysiology*. 2012; (11): 2092-2093
2. Ting Zhao, **Xiaohu Huang**, Liang Han, Xianhua Wang, Heping Cheng, Ruiping Xiao, Ming Zheng. Mitofusin 2 Regulates Cardiac Function Through the Maintenance of Cellular Metabolism. *Circulation*. 2010;122:A21307

HONORS AND AWARDS

- | | |
|-----------|---|
| 2012-2013 | Excellent graduate award of Peking University |
| 2012-2013 | Excellent doctoral dissertation, Peking University |
| 2012-2013 | Award for Research Excellence, Beijing City |
| 2012-2013 | “Gu-Wu” Scholarship for academic excellence of Institute of Molecular Medicine, Peking University |
| 2008-2013 | Scholarship of Peking University (2 nd prize) |
| 2009-2010 | May 4 th scholarship, Peking University |
| 2007-2008 | Award of “Chun-Tsung” scholar |
| 2007-2008 | Excellent undergraduate award of Lanzhou University |
| 2007-2008 | Scholarship of Lanzhou University (1 st prize) |
| 2006-2007 | Scholarship of Lanzhou University (1 st prize) |
| 2007-2008 | National Scholarship |
| 2005-2006 | Scholarship of Lanzhou University (1 st prize) |
| 2004-2005 | Scholarship of Lanzhou University (3 rd prize) |

CONFERENCES ATTENDED

1. PKU-UCSD Forum on Translational Medicine. January 16-17, 2010, Shenzhen, China
2. New horizons in calcium signaling (Volunteer). October 10-13, 2010, Beijing, China
3. 17th International Biophysics Congress (IBC) (IUPAB). October. 30 - November. 3, 2011, Beijing, China
4. The 9th Conference of the Asian Society of Mitochondrial Research and Medicine (ASMRM) & The 5th Conference of Chinese Society of Mitochondrial Research and Medicine (Chinese-Mit). November 2-5, 2012, Beijing, China

MEMBERSHIP IN PROFESSIONAL SOCIETIES:

01/2013-present Member of the International Society for Heart Research (ISHR)

TEACHING EXPERIENCE

03/2009-02/2013 Teaching Assistant
Course name: Scientific Biomedical English Writing

08/2009 and 07/2010 Supervision of summer student
Wenting Guo (current: Peking University)