

CHE-HONG CHEN, Ph.D.

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EDUCATION

National Taiwan University, Taipei, Taiwan, B.S., 1979, Department of Agronomy

University of California, Berkeley, CA. Ph.D., 1986, Department of Genetics

Cornell University, Ithaca, NY, American Cancer Society Postdoctoral Fellow, 1990, Department of Plant Biology

SOCIAL ACTIVITIES

Chair, Board of Directors
Northern America Luke Christian
Medical Mission
北美路加醫療傳道
會董事會主席

Founder, Chairperson, Taiwan
Alcohol Intolerance Education
Society (TAIES)
台灣酒精不耐症衛教協會
創辦人, 理事長

EMPLOYMENT & POSITIONS

Senior Research Scientist (1993-present), Dept. of Chemical and Systems Biology, Stanford University, School of Medicine, Stanford, CA, U.S.A.

CEO, ALDH2 STAR Research Consortium (2015-present)

Visiting Professor (2015-Present), Taipei Medical University, Taipei, Taiwan

Visiting Professor (2016-Present), Fu-Jen Catholic University, Taipei, Taiwan

SPARK Adviser of Translational Research Program, (2015-present), National Taiwan University, College of Medicine, Taipei, Taiwan

SPARK Adviser of Translational Research Program, (2011-present), Stanford University School of Medicine, Stanford, CA, U.S.A.

Co-founder, Aviv Therapeutics, Menlo Park, CA, U.S.A. (2016-)

Co-founder, Consultant, ALDEA Pharmaceuticals, (2011-2015), Redwood City, CA, U.S.A

Molecular Biology Specialist (1992-1993), University of California, San Francisco, Dept. of Neuroscience, San Francisco, CA, U.S.A.

Senior Scientist (1990-1992), Sogetal Biotech Inc. Hayward, CA, U.S.A.

PERSONAL STATEMENT

Dr. Che-Hong Chen, a molecular biologist and geneticist, has been working as a senior research scientist at Stanford University, School of Medicine, for the past 26 years. Dr. Chen's early research includes the characterization of the first intra-cellular receptor for protein kinase C and its protein-protein interaction with other signaling molecules. Dr. Chen's past research interests focused on the role of ethanol-mediated cardioprotection against ischemia-reperfusion injuries. These studies led to his discovery of the important detoxifying function of aldehyde dehydrogenase (ALDH) in the heart. More recently, Dr. Chen has been studying the ALDH gene family and its association with human diseases. By high-throughput screening of small molecule libraries, Dr. Chen pioneered the discovery of a class of novel enzyme activators and inhibitors of aldehyde dehydrogenase. His work has been published in high journals such as *Science*, *Nature Structure and Molecular Biology*, *PNAS*, *Science Translational Medicine* and *Physiological Reviews*. Together with Dr. Daria Mochly-Rosen at Stanford University, Dr. Chen co-founded ALDEA Pharmaceuticals in 2011 and Aviv Therapeutics in 2016 to translate these small molecular ALDH modulators for clinical applications. The ALDH program is currently under development by Foresee Pharmaceuticals based in Taiwan. Dr. Chen's goals are to further understand and to bring these ALDH modulators into therapeutics for human diseases that are associated with reactive and toxic aldehydes. One of the mutations in the ALDH gene family is the common East Asian-specific point mutation of ALDH2 which is present in nearly 560 million people or 8% of the world population and causes the well-known Asian Alcohol Flushing Syndrome. The ALDH2 mutation leads to a deficiency in the capacity of aldehyde detoxification and is associated with high risks of acetaldehyde-induced cancers and other diseases. Using an ALDH2 deficient mouse model, Che-Hong is currently identifying new molecular and pathological targets that are susceptible to toxic and reactive aldehydes. Dr. Chen is an internationally recognized leader in basic and clinical research of aldehyde toxicity and genetic deficiency of ALDH2 and G6PD. He is also an expert in translational research for drug discovery and development and is often invited to speak in the U.S. and other countries including Japan, Brazil, Greece, China and Taiwan. Since 2015, Dr. Chen has initiated and served as the Chief Executive Officer of the Stanford-Taiwan ALDH2 Deficiency Research (STAR) Consortium. The STAR consortium is devoted to the promotion of multidisciplinary international collaboration of basic and clinical research on ALDH2 deficiency and its related diseases between Taiwan and Stanford University. The mission of the consortium also includes public health education and public awareness of ALDH2 deficiency, acetaldehyde toxicity and cancer prevention for the East Asian populations. More recently, Dr. has launched and founded a non-profit, citizen group called Taiwan Alcohol Intolerance Education Society (TAIES) to further advance the goal of ALDH2 deficiency education and public awareness on alcohol-related health issues in Taiwan.

PUBLICATIONS

1. Karoly, CW, Woodman JD, CHEN C-H, Alleman ML, Johns MA and Freeling M (1982) An annotated bibliography of the Adh genes of maize, from 1966 through 1981, and prediction of the future of classical genetics. In: *Maize for Biological Research*, University Press, W. F. Sheridan ed., pp. 145-154.

2. CHEN C-H, Freeling M and Mercklebach A (1986) Enzymatic and morphological consequences of Ds excision from maize Adh1. *Maydica* (Barbara McClintock, Nobel Laureate, commemorative issue) 31:93-108.
3. CHEN C-H, Oishi KK, Kloeckner-Gruissem B and Freeling M (1987) Organ-specific expression of maize Adh1 is altered by a Mu transposon insertion. *Genetics* 116:469-477.
4. Nasrallah JB, Kao T-H, CHEN C-H, Goldberg ML and Nasrallah ME (1987) Amino-acid sequence of glycoproteins encoded by three alleles of the S locus of *Brassica oleracea*. *Nature* 326:617-619.
5. Dwyer KG, Chao A, Cheng B, CHEN C-H and Nasrallah JB (1988) The Brassica self-incompatibility multigene family. *Genome* 31:969-972.
6. Lalonde BA, Nasrallah ME, Dwyer KG, CHEN C-H, Barlow B and Nasrallah JB (1989) A highly conserved Brassica gene with homology to the S-locus-specific glycoprotein structural gene. *The Plant Cell* 1:249-258.
7. CHEN C-H and J. B. Nasrallah (1990) A new class of S-locus sequences defined by a pollen recessive self-incompatibility allele in *Brassica oleracea*. *Molec. Gen. Genet.* 222:241-248.
8. Boyces D, CHEN C-H, Tantikanjana T, Esch JJ and Nasrallah JB (1991) Isolation of a second S-locus related cDNA from *Brassica oleracea*: genetic relationship between the S-locus and two related loci. *Genetics* 127
9. Ron D, CHEN CH, Caldwell J, Jamieson L, Orr E, Mochly-Rosen D "Cloning of an intracellular receptor for protein kinase C; a homolog of the subunit of G proteins." *Proc Natl Acad Sci USA.* 1994; 91(3):839-43.
10. CHEN CH, Gray MO, Mochly-Rosen D "Cardioprotection from ischemia by a brief exposure to physiological levels of ethanol: role of epsilon protein kinase C." *Proc. Natl. Acad. Sci.* 1999; 96:12784-89.
11. Hundle B, McMahon T, Jahan D, CHEN CH, Mochly-Rosen D, Messing R "An inhibitory fragment derived from protein kinase C prevents enhancement of nerve growth factor responses by ethanol and phorbol esters". *J. Biol. Chem.* 1997; 272:15028-35. PMID: 9169479
12. Csukai M, CHEN CH, de Matteis MA, Mochly-Rosen D "The coatmer protein 'cop, a selective binding protein (RACK) for protein kinase C." *J. Biol. Chem.* 1997; 272:29200-06. PMID: 9360998
13. Dorn GW, Souroujon MC, Liron T, CHEN CH, Gray MO, Zhou HZ, Csukai M, Wu G, Lorenz JN, Mochly-Rosen D "Sustained in vivo cardiac protection by a rationally designed peptide that causes epsilon protein kinase C translocation." *Proc. Natl. Acad. Sci.* 1999; 96(22): 12798-803.
14. CHEN CH and Mochly-Rosen D "Opposing effects of delta and epsilon PKC in ethanol-induced cardioprotection." *J. Mol. Cell. Cardiol.* 2001; 33:581-5.
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16. Churchill EN, Murriel CL, CHEN CH, Mochly-Rosen D, Szweda LI "Reperfusion-induced translocation of PKC to cardiac mitochondria prevents pyruvate dehydrogenase reactivation." *Circ. Research* 2005; 97:78-85. PMID:15961716

17. Zhou Q, Cadrin M, Herrmann H, CHEN CH, Chalkley RJ, Burlingame AL, Omary MB "Keratin 20 serine 13 phosphorylation is a stress and intestinal goblet cell marker." *J. Biol. Chem.* 2006; 281:16453-61. PMID:16608857
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- Subclinical Systolic Dysfunction in Large Community-Dwelling Asians. *Alcohol Alcohol*. 2017; 52(6):638-646.
45. Kim J, Shin JH, CHEN CH, Cruz L, Farnebo L, Yang J, Borges P, Kang G, Mochly-Rosen D, Sunwoo JB. Targeting aldehyde dehydrogenase activity in head and neck squamous cell carcinoma with a novel small molecule inhibitor. *Oncotarget*. 2017; 8(32):52345-52356.
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 48. Ueta CB, Campos JC, Albuquerque RPE, Lima VM, Disatnik MH, Sanchez AB, CHEN CH, Medeiros MHG, Yang W, Mochly-Rosen D, Ferreira JCB. Cardioprotection induced by a brief exposure to acetaldehyde: role of aldehyde dehydrogenase 2. *Cardiovasc Res*. 2018 Mar 20.
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P A T E N T S

1. United States Patent No. 7,560,241
Methods for identifying agents that modulate ALDH2 activity
2. United States Patent No. 9,102,651, AU 2008226947, CA 2,679,882, CN 101669030
Mitochondrial Aldehyde Dehydrogenase-2 Modulators and Methods of Use Thereof
3. United States Patent No. 8,124,389
Crystal Structure of Aldehyde Dehydrogenase and Methods of Use Thereof
4. United States Patent No. 8,389,522
Modulators of Aldehyde Dehydrogenase and Methods of Use Thereof
5. United States Patent No. 8,772,295
Modulators of Aldehyde Dehydrogenase and Methods of Use Thereof
6. United States Patent No. 8,354,435
Modulators of Aldehyde Dehydrogenase Activity and Methods of Use Thereof
7. United States Patent No. 8,906,942, EP 2337563B1, STAN-633TW
Modulators of Aldehyde Dehydrogenase Activity and Methods of Use Thereof
8. United States Patent No. 9,273,025

- Mitochondrial Aldehyde Dehydrogenase-2 Modulators and Methods of Use thereof
9. United States Patent No. 9,345,693
Modulators of Aldehyde Dehydrogenase Activity and Methods of Use Thereof
 10. United States Patent No. 9,315,484
Mitochondrial Aldehyde Dehydrogenase-2 Modulators and Methods of Use Thereof
 11. United States Patent No. 9,370,506
Modulators of Aldehyde Dehydrogenase and Methods of Use Thereof
 12. United States Patent No. 9,545,393
Methods and Compositions for Treating Pain
 13. United States Patent No. 9,670,162, CN No.201480025757.4
Mitochondrial Aldehyde Dehydrogenase-2 Modulators and Methods of Use Thereof
 14. U.S. Patent Serial No. 62/536,925 (In Application)
Glucose-6-Phosphate Dehydrogenase (G6PD) Modulating Agents and Methods of Treating G6PD Deficiency
 15. U.S. Patent Serial No. 62/549,849 (In Application)
Monoterpene Activators of Aldehyde Dehydrogenase 3A1 and Methods of Use Thereof
 16. U.S. Patent Serial No. xxx (In Application)
Mitochondrial Aldehyde Dehydrogenase-2 Modulators for Protecting, Expanding and Increasing the Potency of Hematopoietic Stem Cells
 17. JAPAN Application Serial No. 2016-502016
Mitochondrial Aldehyde Dehydrogenase-2 Modulators and Methods of Use Thereof