

Primary Research Areas

SCIENCE AND HUMAN RIGHTS¹

Scientists have an opportunity to make a profound impact by applying their skills to human rights issues.¹ Compelling examples include the application of geographic information systems (GIS) to documentation of atrocities in Darfur² and Physicians for Human Rights revealing an outbreak of cholera in Zimbabwe.³

I serve on the Steering Committee of the American Association for the Advancement of Science (AAAS) Science and Human Rights Coalition, launched in January 2009, and am co-Chair of the Outreach and Communications Committee.

The mission of AAAS Science and Human Rights Program is stated below:

Mission

The AAAS Science and Human Rights Program (SHRP) works with scientists to "advance science and serve society" through human rights. The Program carries out its mission by engaging individual scientists and scientific associations in human rights efforts; applying scientific tools and technologies to enhance human rights work; bringing human rights standards to the conduct of science; and promoting the human right to enjoy the benefits of scientific progress.

We are exploring ways to integrate case studies of human rights issues into both general education and science and mathematics curricula⁴⁻⁸, including involvement of undergraduate students in research.⁶⁻⁷

For more information [click here](#).

Footnotes explanation:

- ¹ Rubenstein, L. and Younis, M., "Scientists and Human Rights," *Science*, 322, 1303 (2008).
- ² www.eyesondarfur.org
- ³ Toney, J.H., "Advancing Human Rights Through Science," *Science*, 324, 176 (2009).
- ⁴ Toney, J.H., Kaplowitz, H., Pu, R., Qi, F., Chang, G., "Science and Human Rights: A Bridge Towards Benefiting Humanity," *Human Rights Quarterly*, Johns Hopkins University Press, **32**, 1008-1017 (2010).
- ⁵ Toney, J.H., Fasick, J.I., Singh, S., Beyrer, C., Sullivan, D.J., Jr., "Purposeful Learning with Drug Repurposing" *Science*, 325, 1339-1340 (2009).
- ⁶ Noguiera, K., Woubneh, W., Toney, J.H., "The Application of Solar Cookers in Food and Water Safety: A Human Rights Project", AAAS Annual Meeting, Bridging Science and Society (2010).
- ⁷ Lafontant, D.E., Woubneh, W., Toney, J.H., "Analysis Of The Design And Efficiency Of The Umbrella And The Panel Solar Cookers And An Introduction Of New Solar Cooker Designs And Efficiency", AAAS Annual Meeting, Bridging Science and Society (2010).
- ⁸ Pu, R., Kaplowitz, H., Toney, J.H. "Science and scientists advancing human rights," AAAS Conference on Transforming Undergraduate Education in Biology: Mobilizing the Community for Change. Washington DC (2009)

TARGETING ANTIBIOTIC RESISTANCE

Identification of metallo- β -lactamase inhibitors

Can the discovery of novel metallo- β -lactamase inhibitors lead to clinically useful compounds capable of reversing antibiotic resistance?

Bacteria have developed several mechanisms of resistance to antibiotics. The reduced permeability of the cell wall, alterations in target enzymes (penicillin-binding proteins), production of biofilms (vide infra) and production of various forms of β -lactamase all contribute to the diminishing effectiveness of antibiotics. Metallo- β -lactamases (MBLs) are zinc metalloenzymes that confer antibiotic resistance to bacteria through the hydrolysis of β -lactam antibiotics. Pathogens that express the enzyme show significantly reduced susceptibility to carbapenems, such as meropenem and imipenem. This project was initiated by my research group in the Department of Biochemistry at Merck Research Laboratories in 1995 in collaboration with medicinal chemists, molecular modelers, microbiologists and protein crystallographers. We studied carbapenem resistance in the clinical pathogens *Bacteroides fragilis* and *Pseudomonas aeruginosa* (*P. aeruginosa*), as well as methicillin-resistant *Staphylococcus aureus* (MRSA).

We previously screened over 2,000 compounds (National Cancer Institute Chemical Diversity Set) for inhibition against IMP-1 MBL and have identified several novel compounds that are capable of reversing carbapenem resistance in a laboratory strain of *E. coli* expressing IMP-1. We have recently extended this approach using a related MBL SPM-1 and are planning to test SPM-1 inhibitors in synergy experiments with meropenem using clinically relevant strains of *P. aeruginosa*. Our current screen is testing for SPM-1 inhibitors in the Johns Hopkins Clinical Compound Library (see: New Uses for Old Drugs) that includes a collection of FDA drugs. This project involves collaboration with Prof. James Spencer at the University of Bristol, UK. Long range plans include collaboration with pharmacologists to study animal models of infection.

DIABETES: STUDYING THE EFFECT OF DIETARY OILS ON INSULIN SECRETION

What is the mechanism of prevention of onset of type 2 diabetes in subjects consuming peanuts?

A study at the Harvard School of Public Health (see: Harvard Study Shows Half Serving of Peanut Butter or Full Serving of Peanuts Eaten Daily Significantly Cuts Risk of Type 2 Diabetes), it was reported that women who consumed at least five ounces of peanuts and peanut butter a week reduced their risk of developing type 2 diabetes by 21% compared to those who rarely consumed peanuts (control group). Another clinical study with high oleic acid peanuts (HOPs, another variety of peanut which has a higher ratio of oleic to linoleic acid), showed improvement of serum lipo-protein profile thereby reducing risk of cardiovascular disease by 14% compared to control. Peanuts are part of the legume family and contain a relatively large amount of healthy types of fat (high in unsaturated fatty acid, approximately 80%, and low in saturated fatty acid, less than 20% and no trans fat) some proteins, antioxidants (e.g., vitamin E, resveratrol), magnesium, potassium, zinc, and phytosterols which could either individually or in combination contribute to the beneficial effects of peanuts. We are addressing the hypothesis of whether components of peanut oil can affect insulin secretion and/or glucose metabolism to explain the clinical benefits of peanuts using both in vitro and in vivo models of diabetes¹⁻². This study was supported by a Cottrell College Science Award from the Research Corporation.

Our interdisciplinary approach exposes undergraduate and graduate students to medicinal chemistry, cell biology, biochemistry and animal pharmacology and could serve as the first

step towards the development of novel compounds with therapeutic properties.

Footnotes explanation:

¹ Chakraborty, G., Thumpayil, S., Lafontant, D.-E., Woubneh, W., Toney, J.H., “Age-dependence of glucose tolerance in adult *KK-A^y* mice: a model of non-insulin-dependent diabetes mellitus,” **Lab Animal, 38**, 364-368 (2009) (Article featured on journal cover)

² Vassiliou, E.K., Gonzalez, A., Garcia, C., Tadros, J., Chakraborty, G., Toney, J.H., “Oleic Acid and Peanut Oil High in Oleic Acid Reverse the Inhibitory Effect of Insulin Production of the Inflammatory Cytokine TNF- α Both In Vitro and In Vivo Systems,” **Lipids in Health and Disease, 8**, 25 (2009). “Highly accessed” article.