



Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: [www.elsevier.com/locate/neures](http://www.elsevier.com/locate/neures)



Perspective

## Valley of death: A proposal to build a “translational bridge” for the next generation

Nao J. Gamo<sup>a</sup>, Michelle R. Birknow<sup>b</sup>, Danielle Sullivan<sup>a</sup>, Mari A. Kondo<sup>a,1</sup>,  
Yasue Horiuchi<sup>a,2</sup>, Takeshi Sakurai<sup>c</sup>, Barbara S. Slusher<sup>d</sup>, Akira Sawa<sup>a,\*</sup>

<sup>a</sup> Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21287, United States

<sup>b</sup> Synaptic Transmission, H. Lundbeck A/S, Valby, Denmark

<sup>c</sup> Department of Drug Discovery Medicine, Medical Innovation Center, Kyoto University Graduate School of Medicine, Kyoto, Japan

<sup>d</sup> Department of Neurology, Johns Hopkins Drug Discovery, Johns Hopkins University School of Medicine, Baltimore, MD 21205, United States

### ARTICLE INFO

#### Article history:

Received 23 September 2016  
Received in revised form 4 November 2016  
Accepted 10 November 2016  
Available online xxx

#### Keywords:

Drug development  
Drug discovery  
Translational research  
Valley of death  
Psychiatric disorders  
Dimensional approach  
Education

### ABSTRACT

There is a great need for novel drug discovery for major mental illnesses, but multiple levels of challenges exist in both academia and industry, spanning from scientific understanding and institutional infrastructure to business risk and feasibility. The “valley of death,” the large gap between basic scientific research and translation to novel therapeutics, underscores the need to restructure education and academic research to cultivate the fertile interface between academia and industry. In this opinion piece, we propose strategies to educate young trainees in the process of drug discovery and development, and prepare them for careers across this spectrum. In addition, we describe a research framework that considers the disease trajectory and underlying biology of mental disorders, which will help to address the core pathophysiology in novel treatments, and may even allow early detection and intervention. We hope that these changes will increase understanding among academia, industry, and government, which will ultimately improve the diagnosis, prognosis and treatment of mental disorders.

© 2016 Elsevier Ireland Ltd and Japan Neuroscience Society. All rights reserved.

### Contents

1. Introduction.....	00
2. Education: institutional level in academia.....	00
3. Education: communication skills and networking.....	00
4. Education: international level.....	00
5. Research framework.....	00
6. Future perspectives.....	00
Acknowledgements.....	00
References.....	00

\* Corresponding author at: The Johns Hopkins Hospital, 600 North Wolfe St Meyer 3-166A, Baltimore, MD 21287, United States.

E-mail address: [asawa1@jhmi.edu](mailto:asawa1@jhmi.edu) (A. Sawa).

<sup>1</sup> Present affiliation: School of Psychiatry, Faculty of Medicine, University of New South Wales, Sydney NSW, Australia.

<sup>2</sup> Present affiliation: Department of Psychiatry and Behavioral Sciences, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan.

<http://dx.doi.org/10.1016/j.neures.2016.11.003>

0168-0102/© 2016 Elsevier Ireland Ltd and Japan Neuroscience Society. All rights reserved.

## 1. Introduction

Major mental illnesses remain significant medical and financial burdens on our society. For example, statistics from the National Institute of Mental Health (NIMH) highlight that there is an annual expenditure of nearly \$58 billion in the United States on mental health (National Institute Of Mental Health, 2006). Since the introduction of chlorpromazine in 1952, current medications in psychiatry still stem from serendipitous findings, are limited in efficacy, and cause substantial side effects (Miyamoto et al., 2012).

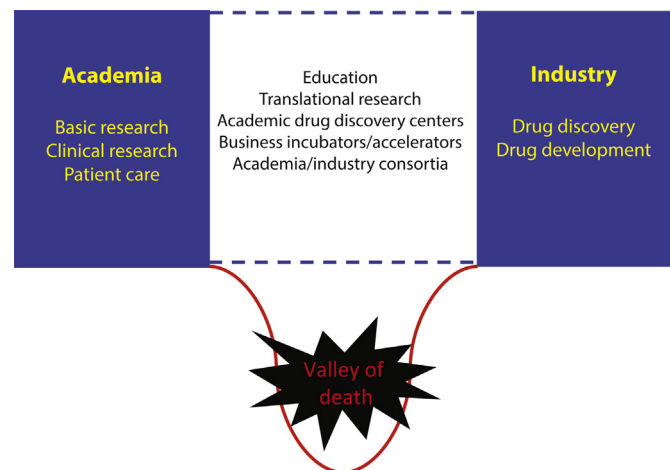
While the need to invest in novel drug discovery for psychiatric disorders is clear, the pharmaceutical industry has been suffering significant business challenges (Choi et al., 2014). Often referred to as the “valley of death,” there is a large gap between basic scientific research and translation to novel therapeutics (Fig. 1). With an estimated cost of \$1–2 billion to develop a new drug, development time lines of 15–20 years, and a failure rate of approximately 95%, many pharmaceutical companies have been forced to downsize their operations, especially in early drug discovery (Slusher et al., 2013). This grim outlook is particularly true for neurological and psychiatric disorders, as the failure rate for experimental drugs for the central nervous system (CNS) is significantly higher than that for other disease areas (Slusher et al., 2013). Indeed, in just the past 5 years, there has been over 50% decline in the number of CNS-focused discovery and development programs in the pharmaceutical industry (Choi et al., 2014). Meanwhile, many academic laboratories do not have sufficient knowledge or infrastructure to translate their findings into commercial or clinical applications.

These problems underscore the need for increased efforts in academic translational research and drug discovery, and making stronger ties with industry. As the interface between industry and academia is potentially fertile ground for initiating discovery for new treatments, it is necessary to narrow the knowledge gap between academic research and translation of findings into novel treatments. In this article, we propose an infrastructure to educate young people in the process of drug discovery and development, encourage translational research that appreciates the underlying biology of mental disorders, and prepare them for careers across academia, industry and government.

## 2. Education: institutional level in academia

How can such training be accomplished? It is important to educate young people in the entire process of developing new drugs. This process encompasses target identification and validation, high-throughput screening, medicinal chemistry, pharmacokinetic and pharmacodynamic analyses, assessment of animal models, preclinical safety assessment and clinical trials, and regulatory approval from the Food and Drug Administration (FDA).

In addition to didactic lectures, immersion in successful cases of drug development, such as for Prozac (Wong et al., 2005) and Clozaril (Crilly, 2007), will help to provide systematic perspectives from preclinical discovery to translational, clinical and regulatory processes. In one example, the Johns Hopkins Drug Discovery Program has recently started teaching a graduate course on drug discovery case studies with lecturers from the pharmaceutical industry (<https://drugdiscovery.jhu.edu/our-courses/drug-discovery-case-studies/>). In addition to these topics, trainees should be educated in medical statistics and the Responsible Conduct of Research (RCR) (Anderson, 2016; Bell, 2015), which will enhance their ability to perform and interpret translational research. It is important to expose young people to a wide variety of translational career options, particularly those outside academia, including government and industry positions. To help them focus their training towards their future career goals, men-



**Fig. 1.** We propose a novel infrastructure for education and research to overcome the “valley of death,” the large gap between basic scientific research and translation to novel therapeutics, and cultivate fertile ground between academia and industry.

tors from these various sectors should help trainees to establish individual development plans (IDPs) from early stages of training. The IDP has become an important concept in academic education (National Institute of General Medical Sciences, 2011), and is particularly important when fostering young trainees at the interface of academia and industry.

It is also critical to support young investigators during the initial steps of turning academic findings into commercial partnerships or new companies. For example, at what stage can an idea be patented, and how does one determine the market opportunity for a particular product? Many academic and business “incubators” and “accelerators” have emerged over the past decade to guide young researchers and entrepreneurs in the early stages of commercialization (Soetanto, 2016). The trainees are provided with the skills and knowledge of intellectual property management, considerations of whether to form a company or license the intellectual property to a larger company, logistics of incorporation, hiring management talent, obtaining the appropriate type of funding at each stage, and writing a business plan, including assessment of the potential market.

## 3. Education: communication skills and networking

This concept differs from traditional M.D./Ph.D. programs, in which medical and research training are simultaneously but separately administered. Instead, we emphasize the continuum from research to drug development. Early efforts in this endeavor include workshops that bring together research and clinical trainees to discuss a topic together from each of their perspectives, such as the “Mind the Gap” workshops at Johns Hopkins University (Posporelis et al., 2014; Sawa, 2014). The goal of such training is to send young people into all sectors involved in translational research and drug discovery and development. The strategy of this approach is to build ties among academic, industry and government experts by helping to understand their complementary roles, and facilitate productive collaborations to ultimately improve the diagnosis, prognosis and treatment of mental disorders.

In an attempt to build a community amongst the growing number of academic drug discovery centers, in 2012, leaders from several centers formed the Academic Drug Discovery Consortium (ADDC) (<http://addconsortium.org/>) (Slusher et al., 2013). Since then, this community has greatly expanded to include over 140 centers and 1500 members worldwide. In addition to an interactive network, this consortium provides opportunities for collaborations

Download English Version:

<https://daneshyari.com/en/article/5739008>

Download Persian Version:

<https://daneshyari.com/article/5739008>

[Daneshyari.com](https://daneshyari.com)