

## Type 2 diabetes, medical knowledge and pharmaceutical innovations.

Da-Yong Lu<sup>1\*</sup>, Jin-Yu Che<sup>1</sup>, Nagendra Sastry Yarla<sup>2</sup>, Hong-Ying Wu<sup>1</sup>, Bin Xu<sup>3</sup>, Shu-Yun Wu<sup>3</sup>, Yi Lu<sup>4</sup>, Ting-Ren Lu<sup>1</sup>, Hong Zhu<sup>5</sup>

<sup>1</sup>Shanghai University, Shanghai, PRC

<sup>2</sup>Divisions of Biochemistry & Chemistry, City University of New York School of Medicine, 160 Convent Avenue, New York, NY10031, USA

<sup>3</sup>Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, PRC

<sup>4</sup>Shanghai Ocean University, Shanghai, PRC

<sup>5</sup>Zhejiang University, Hangzhou, PRC

### Abstract

**Type 2 Diabetes Mellitus (T2DM) is an emerging medical crisis over the past two decades. However, the causality, pathogenesis and therapeutics of type 2 diabetes are currently too refractory to be easily managed in the clinics. Medical knowledge and therapeutic options for T2DM treatments are still of great medical significance. We welcome therapeutics of both cutting-edge and traditional for anti-diabetic treatments in future.**

**Keywords:** Diabetes mellitus, disease causality, anti-diabetic therapy, medical education, type 2 diabetes, cardiovascular complication, traditional chinese medicine.

*Accepted on November 13, 2017*

### Introduction

Type 2 Diabetes Mellitus (T2DM) is an emerging medical crisis over the past two decades. The epidemics of T2DM in China, developing and developed countries have been all growing [1-5]. More importantly, patients with late-stage of T2DM are especially difficult to be reversed. Diabetes causality, pathogenesis, complications, state-of-the-art techniques and other medical options are required for deepening understood. As a tough challenge, following movements must be established. This editorial addresses these types of medical/pharmaceutical explorations.

### Top Challenge

#### *Building global educational systems*

In Most people without medical backgrounds believe that diabetes can be easily prevented from limitations of sweet consumption. In these people's mind, patients with T2DM is caused by eating too much sweet and can be healed by the limitations of sweet consumption. They never expect that T2DM treatment is more than we are imaging. Sweet consumption overdone is only a part of T2DM causalities. Healthy dissemination of medical knowledge of T2DM is indispensable parts of T2DM epidemic managements worldwide. If growing number of people are familiar the knowledge of diabetic causality, pathogenesis and therapeutics, more human beings can benefit from these processes of communicating efforts.

Patients with T2DM may undergo a lethal course, even pathogenesis cascade processes, in susceptible human beings (some of them are family inherit). Yet patients with late-stage of T2DM, their pathogenesis processes and cascade are often difficult to be reversal. Since people with T2DM are commonly asymptomatic at early stages, people must be educated with a range of healthy behavior and high-quality life-styles to

elongate status of live conditions. People should be aware that high calorie food consumption is not the only factor to trigger T2DM, some other unfavorable factors, such as habitually heavy drunk, long-term depression, sleep problem, genetic mutations/variations or sleep apnea, old age etc. [2-11] can also be the culprits of T2DM causality and pathologic processes. Thus, medical checks including blood glucose concentration detection should be regularly undertook for people more than 40 years old.

#### *The type 2 diabetes causalities*

The type 2 diabetes causalities are not fixed; following factors are suggested [2-11];

1. Fetus nutritional insufficient
2. Overfeed or overweight
3. Insulin deficiency and resistance
4. Bad habits (over drunk etc.)
5. Heritage (Genetic or epigenetics)
6. Sleep apnea
7. Lack of enough exercises (Sedentary work)
8. Mental depression
9. Old age
10. Other metabolic causalities (mutual promotion??) and so on

#### *Glucose control agents and clinical therapeutic modality*

Relationship between pathologic pathways and pharmacologic activity of anti-diabetic drug is very useful. In order to promote drug developments and clinical therapies, pathogenesis study of diabetic progress and complications is quite necessary, especially in areas of human heritage characters and genetic

predisposition [12-14]. But it needs time. In initial stage of anti-diabetic explorations, doctors and pharmacologists seek blood glucose control-interfering or sabotaging normal food intake and digestions systems by sugar derivatives. From medical points of views, most of these efforts are relatively superficial because the real pathogenesis causalities of T2DM are mostly insulin-binding or functional-related dysfunction, such as loss functions of pancreas island  $\beta$ -cells [15], liver metabolism [16], insulin resistance [15] and others [17]. According to this view, many in vitro glucose-related studies are especially difficult and off targets. Due to these limitations, diabetic therapeutic study is heat debated.

**Natural chemotherapeutic drug and traditional Chinese medicine (TCM)**

Natural chemotherapeutic drugs commonly have higher therapeutic index against many refractory diseases, such as cancer and viral infections [18-20]. May it also suitable for anti-diabetic therapeutics? However, natural chemotherapeutic drugs are more difficult to be developed comparing with synthetic drugs. To easy this process, TCM are proposed to treat patients with T2DM.

From the views of TCM, type 2 diabetes is likely as symptoms categories of blockage of different important physiological circulations or pathways; include (Tan-Shi-Ti-Zheng, Phlegm wet body disease); (Shi-Re-Ti-Zheng, Damp heat syndrome) or (Xue-Yu-Ti-Zheng, Blood stasis disease). Doctors may prescribe patients with these kinds of herbal soups for different physiological circulations or pathway abnormality.

Besides herbal medicine, some insect products such as propolis are also widely recognized to T2DM treatments in China [10,11]. Propolis is bee extract of waxy-like components extracted from crude honey [21,22]. In China, it was licensed as health-promoting agents yet practiced as blood glucose control for patients with T2DM.

Apart from China, many plant, insect or animal components have also been used for hyperglycemia managements globally.

In Japan, some fermented soy beans (Natto) are also famous for T2DM-induced metabolic complication therapeutics and benefiting [4].

**Drug Combination**

A Drug combination have been successful for a lot of refractory disease managements, such as cancer metastasis [23], HIV/AIDS treatments [24,25] and so on. Since diabetes, especially T2DM can exhibit wider symptoms, variant complications and pathogenic pathways in different individuals, drug combination strategies might be used against every abnormal pathway. A lot of questions should be answered for optimal drug combination utilities in clinical diabetic treatments. It is however still at infancy stage. Currently, even a number of drug combinations have been utilized in clinics, theoretical medical studies are lag behind [26-28]. Now clinical drug combinations are from doctors' empirical and instinct rather than scientifically supported. In future, clinical drug combination should be mathematically analyzed [26-28]. Let's pay more attention on that part of clinical situations.

**Table 1. Major diabetes-induced complications in patients with T2DM.**

Complication locations	Specific types
Metabolic	Cardiovascular (atherosclerosis, hypertension, stroke) Obesity Muscle malformations Infections (chronic skin or leg infections)
Eye complications	Visual damage and blur Cataract Fundus hemorrhages and vessel leakage
Kidney failure	Nephropathy
Cancer	Colon cancer and so on
Brain damage	Brain retardation Cognitive impairments Tiresome feeling and insomnia Lack mental concentrations Mental depression

**Disease complications and treatments**

The Diabetic complications are wide-range, serious across-time and finally life-threatening. Majority of T2DM complications are represented in Table 1. Cardiovascular, nephropathy, visual impairments, mental retardation, chronic leg infections and even cancer can occur in patients with late-staged of T2DM. Thus new generations of T2DM therapeutic agents or drugs for disease complications must be designed and finally licensed in order to improve patient's therapeutic outcomes and survivals (Table 1).

**Future Perspectives**

Presently, except type 1 diabetes, no standard therapeutics is widely used in patients with T2DM. Expensive or cheap drugs are not parallel between their efficacy and toxicity for patients with T2DM. Since growing number of patients are suffered from T2DM and related complications worldwide (doubled morbidity rates over the past two decades), T2DM therapy studies need to be promoted and improved. Persistent efforts and novel ideas are welcome.

High-quality life style and good behaviors, such as regularly physical exercise, early sleep, non-smoking, pay attention to rest and so on will be introduced to patients with T2DM.

Therapeutics study of T2DM is multiple routes and compounds. Among them, natural chemical agents are especially important [17-20]. In order to overcome current therapeutic limitation, reevaluations of past pathologic or therapeutic discoveries in new drug developments are quite necessary.

**Conclusions**

Treatment of patients with T2DM is still a medical challenge for different disease causalities, pathogenesis and complications. We welcome therapeutics of cutting-edge (modern-diagnostics) and traditional (herbal or insulin-related) for anti-diabetic treatments. The importance of educational introductions of T2DM medical knowledge is a good avenue in diabetic epidemic control worldwide.

**References**

1. Yang WY, Lu JM, Weng JP, et al. Prevalence of diabetes among men and women in China. N Eng. J Med. 2010;362:1090-1101.

2. Zimmet PZ, Magliano DJ, Herman WH, et al. Diabetes a 21st century challenge. *Lancet Diabetes Endocrinol.* 2014;2:256-64.
3. Fuchs S, Henschke C, Blumel M, et al. Disease management programs for type 2 diabetes in Germany; a systematic literature review evaluating effectiveness. *Dtsch Arztebl Int.* 2014;111:453-63.
4. Lu DY, Che JY, Yarla NS, et al. Diabetes prevention and treatment , a specific topic for modern medicines. *J Metabolic Syndrome.* 2017;8:231.
5. Thepwoogsa I, Kirby C, Schattner P, et al. Systematic review or meta-analysis type 2 diabetes continuing medical education for general practitioners: what works? A systematic review. *Diabetic Med* 2014; 31:1488-97.
6. Nannapaneni S, Ramar K, Surani S, et al . Effect of obstructive sleep apnea on type 2 diabetes mellitus; a comprehensive literature review. *World J Diabetes.* 2013;4:238-44.
7. Grimaccia F, Kanavos P. Cost, outcome, treatment pathways and challenges for diabetes care in Italy. *GlobalHealth.* 2014;10:58.
8. Wens J, Vermeire E, Hearushaw H, et al. Educational interventions aiming at improving adherence to treatment recommendations in type 2 diabetes. A sub-analysis of a systematic review of randomized controlled trials. *Diabetes Research and Clinical Practice.* 2008;79:377-88.
9. Putta S, Peluso I, Yarla NS, et al. Diabetes mellitus and male aging, pharmacotherapeutics and clinical implications. *Current Pharmaceutical Design.* 2017.
10. Lu DY, Che JY, Wu HY, et al. The pathogenesis and treatments of diabetes, questions and answers. *Cell and Developmental Biology.* 2014;3:e126.
11. Lu DY, Che JY, Wu HY, et al. The pathogenesis and treatments of diabetes, a new insight. *Advanced Techniques in Biology & Medicine.* 2014;2:e102.
12. Rosato V, Tavani A, Gracia-Lavedan E, et al. Type 2 diabetes, antidiabetic medications, and colorectal cancer risks: two case-control studies from Italy and Spain *Front Oncol,* 2016.
13. Asche C, Laffleur J, Conner C, et al. A review of diabetes treatment adherence and the association with clinical and economic outcomes. *Clinical Therapeutics.* 2011;33:74-109.
14. Soleimanpour SA, Gupta A, Bakay M, et al. The diabetes susceptibility gene *Clec16a* regulates mitophagy. *Cell.* 2014;157:1577-90.
15. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and  $\beta$ -cell functions from fasting plasma glucose and insulin concentrations in man. *Diabetologia.* 1985;28:412-19.
16. Maida A, Lamont BJ, Cao X, et al. Metformin regulates the incretin receptor axis via a pathway dependent on peroxisome proliferator-activated receptor- $\alpha$  in mice. *Diabetologia.* 2011;54:339-49.
17. Putta S, Yarla NS, Peluso I, et al. Possible role as multitarget therapeutic agents for prevention and therapy of chronic diseases. *Current Pharmaceutical Design.* 2017.
18. Ali I, Saleem K, Uddin R, et al. Natural products: human friendly anti-cancer medications. *J Egypt Pharm.* 2010;9:133-79.
19. Rumschlag-Booms E, Zhang HJ, Soejarto DD, et al. Development of an antiviral screening protocol: one-stone-two-birds. *J Antivir Antiretrovir.* 2011;7:8-10.
20. Lu DY, Lu TR, Lu Y, et al. Discover natural chemical drugs in modern medicines. *Metabolomics.* 2016;6:181.
21. Lu DY, Che JY. Rethink of diabetes treatment and drug development. *Cell & Developmental Biology.* 2014;3:e125.
22. Wagh VD. Propolis: a wonder bees product and its pharmacological potentials. *Adv Pharmacol Sci.* 2013.
23. Lu DY, Lu TR, Cao S, et al. Drug combinations in cancer treatment. *Clinical Experimental Pharmacology.* 2013;3:134.
24. Pomerantz RJ, Hom DL. Twenty years of therapy for HIV-1 infection. *Nat Med.* 2003;9:867-73.
25. Lu DY, Lu TR, Che JY, et al. New perspectives of HIV/AIDS therapy study. *Recent Patents on Anti-infective Drug Discovery.* 2014;9:112-20.
26. Lu DY, Chen EH, Lu TR, et al. Anticancer drug combinations, studies from different pathways. *Cell & Developmental Biology.* 2015;4:166.
27. Lu DY, Chen EH, Lu TR, et al. Advances in Pharmacoepidemiology & Drug Safety. 2016;55:e138.
28. Lu DY, Chen EH, Wu HY, et al. Anticancer drug combination, how far we can go through? *Anticancer Agents Med Chem.* 2017;17:21-28.

**\*Correspondence to:**

Da Yong Lu  
 Shanghai University  
 PRC  
 Shanghai  
 China  
 Tel: +862166163545  
 E-mail: ludayong@shu.edu.cn