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2017: Beginning of a new era for *Chlamydia* research in China and the rest of the world

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Abstract

The First Chinese *Chlamydia* Research Meeting was held in Lanzhou, China in May 2017, 60 years after the disclosure of reproducible isolation of *Chlamydia trachomatis* by 汤非凡 (Fei-fan Tang). We report current state of the *Chlamydia* research community in China, and briefly review recent progress in *Chlamydia* vaccinology. The meeting represents a new milestone for *Chlamydia* research in the country. The Chinese *Chlamydia* Research Society (CCRS) was formed during the meeting. Future meetings will be held biennially and should facilitate collaboration of Chinese researchers with their domestic and international colleagues.

60 years ago the great medical microbiologist 汤非凡 (Fei-fan Tang, Fig. 1) reported, for the first time in history, reproducible isolation of the trachoma pathogen from eyes of patients in China [1, 2]. The organism, later given the name *Chlamydia trachomatis*, is still the number one infectious cause of blindness in many countries today [3], and also the most prevalent sexually transmitted bacterial pathogen in most geographical areas studied [4]. May 5–8, 2017, some 80 Chinese *Chlamydia* researchers (principal investigators and trainees) gathered in Lanzhou, Gansu to commemorate Prof. Tang's pivotal accomplishment in the history of *Chlamydia* research by sharing their newest research findings at the First Chinese *Chlamydia* Research Meeting (Fig. 2).

The identification of the trachoma pathogen greatly accelerated *C. trachomatis* research worldwide. In response to numerous requests, Prof. Tang sent his *C. trachomatis* isolates to scientists in different countries [5]. He and others soon moved on to test inactivated *C. trachomatis* vaccines. However, results from those studies were disappointing: protection was found to be short-lived and only in some subjects, and vaccination also exacerbated ocular pathology in other subjects following reexposure [6, 7]. Certainly, scientists since those days have appreciated the difficulties in developing effective and safe *Chlamydia*

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vaccines for both ocular and genital infections [8]. Nonetheless, significant progress in *C. trachomatis* vaccinology has been made in recent years. Novel vaccine candidate antigens for humans have been identified [9, 10]. Attenuated organisms have been shown to prevent ocular pathology in nonhuman primates [11]. It has been shown that adjuvants can overcome the need for live organisms for inducing protective immunity in the mouse genital tract [12, 9].

The isolation and initial characterization of *C. trachomatis* earned Prof. Tang well-deserved international recognition. Unfortunately, inside China, Prof. Tang became a victim of political turmoil, and *Chlamydia* research was brought to a complete halt during the Great Revolution starting 1966 around which scientists elsewhere started to recognize that *C. trachomatis* may be a major sexually transmitted pathogen [8]. Substantial *Chlamydia* research was not conducted again there until around the new millennium when some Chinese scientists returned to China after training with overseas *Chlamydia* research groups. Since then, there has been a rapid growth in the Chinese *Chlamydia* research community, which now consists of some 30 independent groups. Almost all these groups have received grants from the National Natural Sciences Foundation. They study different organisms ranging from human chlamydiae (i.e., *C. trachomatis* and *C. pneumoniae*) to animal pathogens, including the newest recognized species isolated from birds and zoonotic pathogens (e.g., *C. psittaci*). Their research subjects include (but are not limited to) basic microbiology, pathogenesis, immunology, vaccinology, molecular epidemiology, and development of new therapeutics and diagnostic methodology.

Attendees of the meeting reached an agreement to form the Chinese *Chlamydia* Research Society (CCRS). Officers of the first CCRS council are as follows:

President: Quanzhong Liu

Secretary/treasurer: Yuanjun Liu

Councilors: Hong Bai, Cheng He, Erguang Li, Zhongyu Li, Lihua Song, Lingli Tang, Yimou Wu, Yueping Yong, Ping Yu, Lifang Zhang, Lijun Zhang, Weiming Zhao, Heping Zheng, and Jizhang Zhou

Foreign Councilors: Francis Eko (USA), Huizhou Fan (USA), Ming Tan (USA), Xi Yang (Canada), and Guangming Zhong (USA)

It was agreed that CCRS will hold biennial meetings to facilitate information dissemination and to catalyze research collaboration. CCRS welcomes foreign scientists to participate in its biennial meetings (five scientists who have foreign citizenships and work in the US and Canada, listed above, attended this first meeting).

Some meeting attendees noticed that the Chinese Centers for Disease Control and Prevention (China CDC) and the healthcare industry do not pay sufficient attention to surveillance and diagnosis of ocular and sexually transmitted chlamydial infections. Most hospitals do not test for *Chlamydia* at all while others inappropriately use antichlamydial antibody detection as a diagnostic means. *C. trachomatis* nucleic acid tests are offered in few places. It is well established that missed diagnosis is associated with missed or improper

treatment, leading to increased risks of infertility, pelvic inflammatory disease and other complications [8, 13].

60 years is a full circle in the Chinese calendar. 2017 means a new beginning for both Chinese and international *Chlamydia* researchers. Compared to their colleagues in the US and other developed countries, *Chlamydia* researchers in China have additional tasks to do. They need to urge China CDC to come up with a surveillance program to guide the government to develop preventive programs. They should also urge healthcare institutions to adopt proven effective diagnostic tools to guide clinicians to treat patients effectively.

Internationally, despite intense efforts, developing safe and effective *C. trachomatis* vaccines for humans remains challenging [8, 13]. A better understanding of *C. trachomatis* immunology [14–16] and microbiology [17, 18] should greatly facilitate the process. The frequent detection of non-lymphogranuloma venereum serovars of *C. trachomatis* in the human gastrointestinal tract [19] but lack of association with pathology [20], and the induction of transmucosal immunity by non-pathogenic colonization of *C. muridarum* in the mouse gastrointestinal tract ([21] & unpublished observation) may have significant implications for *C. trachomatis* vaccinology. Newly developed genetic tools has already greatly accelerated *Chlamydia* research [22, 23, 21, 24, 25]. Undoubtedly, they will also speed up *C. trachomatis* vaccinology (e.g., Fig. 3). Hopefully, a much shorter time than another 60 years will be needed to have effective preventive strategies developed and implemented, and *C. trachomatis* researchers can direct their efforts at other health problems.

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Fig. 1.
Prof. Fei-fan Tang on a commemorating stamp issued by China Post in 1992.

Fig. 2.
Group photo for the attendees of the First Chinese *Chlamydia* Research Meeting.

Fig. 3. Imaging luciferase-expressing chlamydiae 70 days after intragastric inoculation. Left: whole-body imaging of a live animal. Right: *ex vivo* imaging of different organs. The enterically infected mice were found to develop robust antichlamydial immunity in the genital tract (unpublished observation).