

IP PROTECTION OF PREVENTIVE TCM AND PRECISION MEDICINE IN CHINA

HARNESSING HOLISTIC RESEARCH FROM MAN TO MANKIND

Suggested citation:

Danny Friedmann, IP Protection of Preventive TCM and Precision Medicine in China, Harnessing Holistic Research from Man to Mankind, special number MEDICINE AND LAW (WAML), forthcoming 2018.

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Abstract: Prevention is better than to cure. This was acknowledged in Ancient China, where traditional Chinese medicine (TCM) tried to re-harmonise people by taking a holistic view on health and going after the root of the disease not just the symptoms. The Chinese government views TCM as complementary to Western medicine and invests heavily in its research, promotion and protection via patent law, trade secrets and geographical indications. China would also like to and could dominate the developments in precision medicine, by sequencing the genomes of millions of its people. This knowledge will make it possible to go after the root of diseases, via the identification of genetic markers, and remove the roots of these diseases via gene editing technology. Patent law could harness the efforts to identify the genetic markers by giving incentives to researchers, or harm the developments in regard to gene editing technology, as might be caused by an overcrowded patent landscape.

Keywords: intellectual property; patent law; trade secret; geographical indication; precision medicine; preventive medicine; traditional Chinese medicine; CRISPR-Cas9; genetic markers; China.

1. INTRODUCTION

“A doctor who treats disease after it has happened is a mediocre doctor. A doctor who treats a disease before it has happened is a superior doctor.”

Yellow Emperor, CLASSIC OF INTERNAL MEDICINE, 2 century BC

Traditional Chinese Medicine (TCM)¹ can be seen as an effort to develop a precision medicine *avant la lettre*, accurate and personalised. In TCM the preventive medicines are at least as important as the therapeutic medicines. With the advances made in genetics and genomics,² Western evidence-based medicine is moving towards preventive treatments as well.³ There is a paradigm shift going on in the medical world from “reactive, disease-oriented medical culture toward a proactive, health-based one.”⁴ In addition, there is a growing trend of people that proactively diagnose themselves using health tracking technology: sensors coupled with for example smartphones, whereby they can tap into powerful artificial intelligence (AI) that can analyse and compare their data, dynamically over time, and in comparison with a larger population; recognise patterns and make predictions.⁵ Besides for genetics and genomics, AI can be

¹ Article 2 TCM Law provides a definition of TCM: “the general term of medicine of all Chinese ethnic groups including the Han ethnic group and minority ethnic groups, reflects the understanding of the Chinese nation on life, health and diseases, and is a medicine and pharmacology system with long historical traditions and unique theories and technical methods.” TCM Law of the PRC, 2017 issued by the Standing Committee of the National People's Congress, Order No. 59 of the President, 25 December 2016, effective 1 July 2017, available at: http://www.npc.gov.cn/npc/xinwen/2016-12/25/content_2004972.htm. [28 November 2017]

² WHO definitions of genetics and genomics, WHO, available at:

<http://www.who.int/genomics/geneticsVSGenomics/en/>. [28 November 2017]

³ Hood L & Friend S 2011, ‘Predictive, personalized, preventive, participatory (P4) cancer medicine’, *Nat Rev Clin Oncol*, vol. 8, no. 3, pp. 184-187. Available at: <https://www.nature.com/articles/nrclinonc.2010.227>. [28 November 2017]

⁴ Reynolds T 1998, ‘Putting prevention into practice: The physician's role’, *Ann Intern Med*, vol. 129, no. 8, pp. 679–680. Available at: <http://annals.org/aim/article-abstract/711768/putting-prevention-practice-physician-s-role>. [28 November 2017]

⁵ Hagan P 2016, ‘Can an app really help you spot a risky mole? SkinVision can help you 'be your own doctor' by finding irregularities’, *Daily Mail*, 17 October. Available from: <http://www.dailymail.co.uk/health/article-3845614/Can-app-really-help-spot-risky-mole-SkinVision-help-doctor-finding-irregularities.html>. [28 November 2017] Dormehl L 2016, ‘New algorithm could help diagnose depression by analyzing the tone of your voice’, *Digital Trends*, 12 July. Available at: <https://www.digitaltrends.com/cool-tech/machine-learning-depression-detection/>. [28 November 2017]

used in relation to transcriptomics-,⁶ proteomics-,⁷ and blood biochemistry-based biomarkers of multiple diseases, and analytical tools for high-throughput⁸ screening.⁹ An AI programme developed in New York read millions of electronic medical records and was able to identify patterns in connections and associations to predict diseases not detected by doctors.¹⁰

In Ancient China, the more wealthy people paid their TCM doctor a retainer to keep them healthy. If the patient became sick, the doctor would not be paid until the patient's health returned.¹¹ Western medicine is migrating in this direction. Value-based care is focused on preventing diseases and maintaining health, it increases the number of quality life years and is beneficial for the individual and society at large.¹² Therefore, there should be sufficient incentives in the medical world to develop these preventive medicines. The PRC views TCM as complementary and an affordable alternative to Western medicine. In hospitals in the PRC, Macau and Hong Kong, the top floor is often exclusively reserved for TCM medicine, while they also mix Western medicine with TCM.¹³

Section 2. deals with how the Chinese government promotes preventive medicine and how it upgraded the position of TCM in comparison with Western medicine. The protection of intellectual property (IP) seems to be an indispensable condition to an effective promotion of preventive medicine, modern and ancient.

Section 3 covers the options of how to protect TCM via IP. Some of TCM's idiosyncratic characteristics make the protection via patent law extremely challenging. Sometimes the protection of trade secrets can offer a solution.

⁶ Transcriptomics: study of the complete set of RNA transcripts that are produced by the genome.

⁷ Proteomics: large-scale study of proteomes. A proteome is a set of proteins produced in an organism, system or biological context.

⁸ High-throughput research can be defined as the automation of experiments.

⁹ Takeshi, K 2016, 'Upcoming challenges in intellectual property presented by emerging pharmaceutical technologies', PHARM. PAT. ANAL. vol. 6, no. 1, pp. 1–4, available at: <https://www.future-science.com/doi/pdf/10.4155/ppa-2016-0040>. [28 November 2017]

¹⁰ Chan, K, et al. 2013, 'An Empirical Analysis of Topic Modeling for Mining Cancer Clinical Notes', 2013 IEEE 13th International Conference on Data Mining Workshops, Dallas, TX, pp. 56-63, <http://ieeexplore.ieee.org/document/6753903/authors?ctx=authors>. [28 November 2017]

¹¹ Daemmrich, A 2013, 'The political economy of healthcare reform in China: Negotiating public and private', SpringerPlus vol. 2, no. 1, p. 3. Available at: <http://www.springerplus.com/content/2/1/448>. [28 November 2017]

¹² Illness is expensive for society: the patient stops working, needs hospitalization and costly curative medicines.

¹³ For example an operation can be accompanied by acupuncture to locally anaesthetise the patient.

Section 4. focuses on the challenges to protect genetic markers and genome editing technology via patent law. The challenge of the first category is predominantly caused by patent eligibility standards of the subject matter. The challenge of the latter category could be the emergence of patent thickets that could stifle further research.

Section 5. gives the conclusions.

2. PRC'S VIEW: TCM VERSUS WESTERN MEDICINE

Since Xi Jinping came into power as General Secretary of the Communist Party of the PRC in 2012, he has been insisting that TCM should be given equal status to Western medicine. TCM is affordable, holistic and last but not least Chinese, thus patriotic. The equality in status of TCM and Western medicine was codified in the first TCM Law in 2016.¹⁴ This law promotes the development of TCM,¹⁵ guarantees Chinese citizens access to TCM,¹⁶ and commits to protect the IP of TCM.¹⁷ In 2017 the State Council went a step further than equalizing the status of TCM to Western medicine:

“We should improve the system for Western medicine to learn from TCM. We should encourage clinical graduates to further their studies in TCM, and encourage doctors adopting Western medical practices to leave their positions and study TCM.”¹⁸

¹⁴ Article 3, *supra* footnote 1.

¹⁵ *Ibid.*

¹⁶ *Ibid.*, Article 6.

¹⁷ *Ibid.*, Article 8.

¹⁸ Article 11 last sentence, Opinions on Deepening Medical Cooperation on Further Promoting the Reform and Development of Medical Education, General Office of the State Council, Guo Ban Fa [2017] No. 6, 11 July 2017. Available at: http://www.gov.cn/zhengce/content/2017-07/11/content_5209661.htm. [28 November 2017]

The State Council's call to even abandon Western medicine positions in favour of TCM, was met by criticism on social media such as Weibo,¹⁹ but demonstrates that the Chinese government takes the promotion of TCM to the Chinese population and the world very serious.

In 2016, the State Council, had already issued the Strategic Outline for the Development of Chinese Medicine in February 2016.²⁰ Teaching TCM to primary and middle school students is listed as a goal to be achieved by 2030. Zhejiang is the first province where TCM learning is already compulsory for primary school children.²¹

In 2017, the State Council announced that TCM services will be accessible in all existing community-level health service centres around the PRC.²² The PRC is heavily investing in TCM institutes, such as the TCM Science and Technology Industrial Park of Co-operation between Guangdong and Macao, located in Macau.²³ At the end of 2015, there were 4,000 hospitals in the PRC that offered TCM, compared to 2,500 TCM hospitals in 2003. The number of licensed practitioners in the PRC has increased by almost 50%, to more than 450,000. The PRC is also subsidising the teaching of TCM via Confucius Institutes abroad.²⁴

¹⁹ Feng, J 2017, 'A backlash against promotion of traditional Chinese medicine – China's latest society and culture news', *SupChina*, 14 July. Available at: <http://supchina.com/2017/07/14/backlash-promotion-traditional-chinese-medicine-chinas-latest-society-culture-news/>. [28 November 2017]

²⁰ Outline of the State Council on Issuing the Strategic Planning for the Development of Traditional Chinese Medicine (2016-2030), 22 February 2016. Available at: http://www.gov.cn/zhengce/content/2016-02/26/content_5046678.htm. [28 November 2017]

²¹ 'Why do primary school students have to learn TCM?', *Qianjiang Evening News*, 12 September 2017. Available at: http://qjwbepaper.qjwb.com.cn/html/2017-09/12/content_3569705.htm?div=-1. [28 November 2017]

²² Reform Notice of 2017, General Office of the State Council on Issuing the Deepening Medical and Health System, publication [2017] No. 37, 25 April 2017. Available at: http://www.gov.cn/zhengce/content/2017-05/05/content_5191213.htm?from=timeline&isappinstalled=0. [28 November 2017]

²³ Phase 1: headquarters, a testing and research centre and a GMP Pilot Plant. 2.3 billion RMB was invested in Phase I, and which will come into use by 2017. Phase 2: medical testing, research and constructing support facilities for GMP production; healthcare services and training hub for Chinese medical practice.

²⁴ 'China is ramping up its promotion of its ancient medical arts', *The Economist*, 31 August 2017. Available at: <https://www.economist.com/news/leaders/21727907-dangerous-humans-well-rhinos-china-ramping-up-its-promotion-its-ancient>. [28 November 2017]

The promotion of TCM is also political and a sign of appreciation of Chinese culture.²⁵ Sometimes TCM is equated with patriotism while Western medicine is equated with treason.²⁶ In this vein, it is intolerable for the PRC to accept that, because of insufficient IP protection of its TCM, countries such as Japan and South Korea are taking over the TCM market internationally,²⁷ without a revenue stream going back to the PRC. At least Japan and South Korea used to source the ingredients from the PRC, but these countries have begun to source the TCM herbs outside the PRC.²⁸

In 2015 the then US President Barack Obama launched the Precision Medicine Initiative, a US\$215 million funding commitment aimed at ‘pioneer[ing] a new model of patient-powered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients’.²⁹ In 2016, the PRC’s president Xi Jinping announced the China Precision Medicine Initiative,³⁰ a US\$9.2-billion, 15-year project.³¹

The study of genetics helps to find mutations on a single gene (which is a block of DNA which encodes proteins, and proteins dictate cell function)³² and could cause a certain disease. However, diseases are often

²⁵ “Mr Xi’s efforts are motivated in part by politics. He wants to be seen as an ardent patriot and champion of Chinese culture.” *Ibid.*

²⁶ Tu, Y & Ochs, S 2014, ‘Interchange and Conflict Between Traditional Chinese Medicine and Western Medicine’ in Fang, T (ed) *History and Philosophy of Chinese Medicine*, p. 204.

²⁷ Japan and South Korea dominate the production of TCM 80 percent; the PRC produces only 5 percent. Guo, C 2017, ‘Traditional Chinese Medicine? 100% Made In Japan’, *WorldCrunch*, 30 March. Available at: <https://www.worldcrunch.com/business-finance/traditional-chinese-medicine-100-made-in-japan>. [28 November 2017]

²⁸ *Ibid.*

²⁹ The White House, Fact Sheet: President Obama’s Precision Medicine Initiative, 30 January 2015, available at: <https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative>. [28 November 2017]

³⁰ The project will collect DNA samples and data from 4,000 volunteers over four years. “In addition, they will conduct precise medical research on 2,000 of the volunteers, including whole genome sequence analysis and genome health, with the aim of early warning and intervention analysis.” Precision medicine, *China Daily*, 18 January 2016, available at: http://www.chinadaily.com.cn/opinion/2016-01/18/content_23126509.htm. [28 November 2017]

³¹ Russell, G 2016, ‘China plans leading role in ‘precision medicine’ field,’ *Reporting Health & Medicine*, 6 March. Available at: <http://imsc.hku.hk/reportinghealth2016/2016/04/06/china-plans-leading-role-in-precision-medicine-field/>. [28 November 2017]

³² Humans have about 24,000 functional genes and about 120,000 genes that do not seem to function but represent the archival history of how we used to function as a species.

complex and caused by an interplay of the genes of an organism.³³ Genomics studies the differences in all of the genome and what these differences contribute to its characteristics. By going through billions of DNA units in a population, making use of big data, computational power and AI, one can identify specific gene-mutations and their links to certain diseases.

The PRC set up its first national gene bank in 2016,³⁴ and is also investing heavily in precision medicine via the China National Genebank; more than US\$200 million to more than 100 projects. As mentioned above it plans to spend more than US\$9 billion on the program up through 2030. Between 2016 and 2020 it would like to have sampled the genes of one million people.³⁵ Jiangsu province has announced that it will sequence one million genomes.³⁶ After having sequenced millions of genomes, China might be in a better position than the US to identify mutations, because of its larger populations of patients for each disease.

Without sequencing someone's genome, it is sometimes possible to infer from someone's family history a risk profile.³⁷ If the risk for certain diseases is identified then one can adapt one's diet and lifestyle to decrease the chances that a disease will manifest itself. On the other end of the spectrum, after mapping the genome, a single error out of three billion bases of the genome can be corrected. The latter took already place on an embryo at the Sun Yat-sen University in Guangdong, PRC in 2017.³⁸ However, heavy clouds

³³ A human genome consist of 3.2 billion base pairs (variations of Adenine-Thymine and Cytosine-Guanine).

³⁴ Zhang, P 2016, 'China opens first national gene bank, aiming to house hundreds of millions of samples', *SCMP*, 22 September. Available at: <http://www.scmp.com/news/china/article/2021623/chinas-noahs-ark-first-national-gene-bank-opens-shenzhen>. [28 November 2017]

³⁵ Cyranoski, D 2016, 'China's bid to be a DNA superpower', *Nature*, 22 June. Available at: http://www.nature.com/news/china-s-bid-to-be-a-dna-superpower-1.20121?WT.feed_name=subjects_biotecnology. [28 November 2017]

³⁶ Geib, C 2017, 'A Chinese Province Is Sequencing One Million of Its Residents' Genomes', *Futurism*, 8 November. Available at: <https://futurism.com/chinese-province-sequencing-1-million-residents-genomes/>. [28 November 2017]

³⁷ Mikail, C 2003, 'Genetics and preventive medicine: Beyond family history', *Genetics in Medicine* no. 5, p. 407. Available at: <https://www.nature.com/articles/gim2003364>. [28 November 2017]

³⁸ Liang, P *et al.* 2017, 'Correction of β-thalassemia mutant by base editor in human embryos', *Protein Cell* no. 8, p. 811.

are packing together on the horizon. There are fierce patent disputes going on in the US and China over CRISPR–Cas9,³⁹ the system that makes identifying and cutting the DNA reliable and efficient.⁴⁰

3. PROTECTION OF TCM VIA IP

TCM can be protected via different legal instruments such as the protection of Traditional Knowledge (TK), Patent Law, Trade Secrets and Geographical Indication (GI). Unfortunately the development of TK law seems to be stalled. With patent law, the novelty, inventiveness and utility are the requirements that make protection of TCM so arduous. The protection via GI does not always make commercial sense, and the protection via trade secrets, including via *sui generis* systems, have their own challenges.

TK

TCM is doctrinally part of TK,⁴¹ which is being developed by two fora: the Convention on Biological Diversity (CBD) and WIPO's Intergovernmental Committee on IP and Genetic Resources, Traditional Knowledge and Folklore (IGC).

TK refers to the knowledge systems of indigenous peoples, collectively owned, reflective of their identity, it is evolving, and often not protected by the conventional IP system. It includes folklore, traditional cultural expressions, these are cultural expressions manifested in music and dance, design, architecture, symbols. The other end of the spectrum: technical knowledge and knowhow, related to biodiversity, healthcare and agriculture. There are examples where pharmaceutical companies have exploited the knowledge, have developed inventions, drugs for example, and patented them without the indigenous people being aware. A question often raised with TK is who should benefit from the protection? Should the indigenous peoples be the rightholders directly, or should the state hold these rights on their behalf. Should it be an exclusive right,

³⁹ Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR associated protein 9 (Cas9) is genome editing technology.

⁴⁰ *Board Institute, Inc. v UC Berkeley and U of Vienna*, PTAB, 15 February 2016, p. 2. Available at: <http://www.ipwatchdog.com/wp-content/uploads/2017/02/CRISPR-ruling-02-15-2017.pdf>. [28 November 2017]

⁴¹ Hughes, J 2013, 'Traditional Knowledge, Cultural Expression, and the Siren's Call of Property', *San Diego Law Review* No. 49, p. 1215, *passim*. Available at: <https://ssrn.com/abstract=2215996>. [28 November 2017]

or a compensation and acknowledgment? Is prior informed consent needed before using the TK?⁴²

Unfortunately the development of the TK in the form of CBD and IGC have stalled.

Patent Law

The rationale of patent law is to grant inventors a temporary monopoly in exchange for disclosure of the invention, so that the inventor is incentivized to invent and raise the state of art.

Article 2 Patent Law of the PRC⁴³ provides the definitions of invention and utility model: An invention is a new technical solution relating to a product, process or an improvement thereof; and utility model is a new technical solution relating to the shape, structure or a combination of shape and structure of a product which is fit for practical use. Article 22 Patent Law of the PRC⁴⁴ clarifies that an invention or utility model in the PRC must meet the following patentability requirements: novelty, inventiveness and usefulness.

Novelty

TCM, the holistic healing and health concept that passed from generation to generation for over thousands of years, recognises that each patient is fundamentally unique and also changing. TK, whether it exists in oral or written form constitutes prior art and therefore destroys novelty for any medicines based on this TK.⁴⁵ An example is Qinghao = Sweet Wormwood (*Artemisia annua*), as a medicine against malaria. In 1967, Mao Zedong asked Tu Youyou to find a medicine against malaria. By researching ancient TCM texts

⁴² Wendland, W 2011, *Interview by Dr. Shlomit Yanisky-Ravid, Director, Comparative Legal Research Center at Ono Academic College, International Conference: Intellectual Property Law and Development -- the Road Ahead*, Traditional Knowledge and Access to Knowledge was held at Ono Academic College on October 24-25, 2011, YouTube video, November 1. Available at: <https://www.youtube.com/watch?v=-fLQghh7Ful>. [28 November 2017]

⁴³ Patent Law of the PRC, Decision of the Standing Committee of the National People's Congress on Amending the Patent Law of the PRC, adopted at the 6th Meeting of the Standing Committee of the Eleventh National People's Congress on December 27, 2008, is hereby promulgated and went into effect on 1 October 2009, available at: <http://www.wipo.int/edocs/lexdocs/laws/en/cn/cn028en.pdf>. [28 November 2017]

⁴⁴ *Ibid.*

⁴⁵ Other ancient TCM texts that constitute prior art and thus destroy novelty: Huang Di Neijing, 'Inner Canon of the Yellow Emperor', between the Warren States 475-221 BC and the Han Dynasty 206 BCE-220 CE; Shang Han Za Bing Lun, 'Treatise on Cold Diseases and Miscellaneous Diseases', 150-219 CE; Shen Nong Ben Cao Jing, 'The Classic of Herbal Medicine', 200-250 CE.

Tu came across the Handbook of Prescriptions for Emergency Treatments written by Ge Hong in 340 CE, which includes: “Take one bunch of Qinghao, soak in two sheng (around 0.4 L) of water, wring it out to obtain the juice and ingest it in its entirety.” Tu modified the procedure until it had anti-malarial characteristics. Due to the lack of novelty, Qinghao, was not patentable. Tu did win the Nobel Prize of Medicine in 2015.

Inventiveness

According to Article 22 Patent Law of the PRC,⁴⁶ the invention has prominent and substantive features and represents notable progress, or the utility model possesses substantive features and represents progress. However, the efficacy of most of TCM medicines has not been proven according to Western standards. Some researchers test TCM compounds’ efficacy on populations instead of one person. This is in contradiction to TCM’s philosophy which aims to use the right medicine, in the right dosage for a particular person to bring his or her whole body back to harmony. In contrast, Western evidence-based theory tests *in vitro* or *in vivo* and does clinical tests that simulate the effect that a compound or biological substance has on an organ.

Taiwan is the only jurisdiction where TCM philosophy is recognised in a legal text: Guideline for examining Chinese Herbal Medicine patent applications.⁴⁷ The Guideline states that the medical effect of a TCM prescription can be proved by TCM theory, as long as a person having ordinary skill in the art (PHOSITA) recognises its medical function.⁴⁸ Therefore, under the Taiwanese patent regime, a medicine is effective if a PHOSITA determines that it increased the Qi or the Yin and thus decreased the Yang or

⁴⁶ *Supra* footnote 43.

⁴⁷ Hsiao, J Patent 2007, ‘Protection for Chinese Herbal Medicine Product Invention in Taiwan’, *Journal of World Intellectual Property* vol. 10, no. 1, pp. 1–21, 7-13, available at: <http://onlinelibrary.wiley.com/doi/10.1111/j.1422-2213.2007.00311.x/pdf>. [28 November 2017] Kuo, Y & Chen C 2008, ‘International report - First patenting guidelines for traditional Chinese medicine’, *IAM magazine*, 16 January. Available at: <http://www.iam-media.com/reports/Detail.aspx?g=0cdc3c63-988e-49b3-b8c4-de09283e755c>. [28 November 2017]

⁴⁸ *Ibid*, at 12-13.

vice versa; or that the pattern has changed for the better in regard to the Bian Zheng Lun Zhi.⁴⁹ In TCM theory, medical treatment is directed at the roots of the disease, which may be located in parts of the body other than where the symptoms manifest themselves. Therefore, if the medicine effectively treats the root part of the body, than the PHOSITA in Taiwan could consider the medicine to be effective.⁵⁰

Utility

TCM theory distinguishes between single herb prescriptions (*danfang*) such as the abovementioned Qinghao, or multiple herb prescriptions (*fufang*). If the *danfang* is novel and inventive, then there is no problem to get patent protection. In contrast, a *fufang* may consist of many chemical elements, and the chemical interaction between the ingredients is often complex and unclear. For a lack of better prescriptions, *fufang* are defined as chemical and physical properties (where the solubility, melting point *etc.* are described). The herb or combination of herbs are often considered to be more effective than one or more active ingredients of the herbs.

Disclosure

Article 26(3) Patent Law of the PRC specifies the requirement for sufficiency of the disclosure: “The written description shall contain a clear and comprehensive description of the invention or utility model so that a technician in the field of the relevant technology can carry it out”.⁵¹ However, this sufficient disclosure requirement is a problem because the medical prescriptions of TCM vary according to the specific conditions of the patient. Then, since the natural conditions under which the medicinal herb is growing influences the biodiversity of the medicinal ingredients, specific conditions are prescribed such as climate, geology, soil, hydrology, vegetation, biology, *etc.* Both the uniqueness of the patient and the lack of stability

⁴⁹ Pattern differentiation and treatment determination: the view that a certain pattern of disease is the reflection of a disorder of the human organism

⁵⁰ TCM uses a different taxonomy. The body is divided in liver, heart, spleen, lung and kidney. But each encompasses more than just the organ. For example the lung relates closely to the body-fluid metabolism, to blood circulation, and to the nervous and immune systems, as well as to the respiratory function.

⁵¹ *Supra* footnote 43.

and homogeneity of the quality and conditions for the medicinal herbs make that the prescriptions for a TCM are weakly defined and delineated. Thus it is very difficult if not impossible to disclose the TCM for the patent applicant and very difficult if not impossible to reproduce a particular medicine for the PHOSITA. An additional problem is that TCM is a comprehensive system of balance, harmony, moderation and prevention together with the medicinal herbs. Since the medicine is interwoven with for example a change in lifestyle, it is hard to determine what exactly caused the improvement.

Claims that a *fufang* prescription is effective to treat multiple diseases often impede patent applications. Therefore, *fufang* prescriptions that are often not patentable as a patent outside the PRC; are often patentable in the PRC by redrafting them as product-by-process, method of processing, method of administration or new use claims.

Trade Secret

TCM formulas that are still kept secret can be protected via trade secrets. Article 10 Law against Unfair Competition of the PRC⁵² defines a trade secret as: “technical and operational information which is not known to the public, which is capable of bringing economic benefits to the owner of rights, which has practical applicability and which the owner of rights has taken measures to keep secret.”⁵³

In ancient times the TCM master would pass his secret formulas to the next generation. Often the formulas were encrypted and the methods of interpretation were orally passed on. To keep formulas of successful medicines secret for centuries is difficult. Therefore this method seems more suitable for small scale production and treatment, so that not too many people have to know the secret ingredients and procedures.

⁵² Law against Unfair Competition of the PRC, adopted by the Third Session of the Standing Committee of the Eighth National People's Congress on 2 September 1993 and came into force on 1 December 1993. Available at: <http://www.wipo.int/edocs/lexdocs/laws/en/cn/cn011en.pdf>. [28 November 2017]

⁵³ *Ibid.*, Article 10 also provides four acts that constitute trade secret infringement: 1. Obtaining trade secrets from the owner by stealing, promising gain, using coercion or other improper means; 2. Disclosing, using or allowing others to use trade secrets obtained by stealing, promising gain, using coercion or other improper means; 3. Disclosing, using or allowing others to use trade secrets that a party has obtained by breaking an agreement or disregarding the requirements of the trade secret owner to maintain the trade secret in confidence; 4. Where a third party obtains, uses or discloses someone else's trade secret when he had, or should have had, awareness of the illegal acts mentioned above.

This method is not conducive for industrialization and export. Export markets require disclosure as medicine, but as food which has a lower disclosure requirement this is more possible.

Coca-Cola's Company's secret recipe for Coca-Cola syrup is the poster child of the protection via trade secrets, since 1891.⁵⁴ PRC's commercially successful secret TCM formula that not been reverse-engineered is Yunnan Baiyao. In 1996, the State Secrecy Committee of the State Council decreed that the Yunnan Baiyao prescription and its manufacturing craft is to be listed and protected as national top-secret information.⁵⁵

The PRC has 55 minorities plus the dominant Han. Many of these minorities have developed their own ethnic TCM. And some of these medicines are still kept secret.⁵⁶

Sui generis

To promote those TCMs that are not patentable, but deserve protection, the State Council introduced a *sui generic* regulation covering the specific subject matter of TCM: Regulations on the Protection of TCM (TCM Regulations) which became effective on 1 January 1993.⁵⁷ The TCM Regulations distinguish between first and second class protection of TCM. Only the prescriptions and pharmaceutical techniques of types of TCM under first class protection shall be kept secret and shall not be published by the producing enterprises having been granted the Certificate of Protection of Types of Traditional Chinese Medicine, during the term of protection, according to Article 13 TCM Regulations.⁵⁸

⁵⁴ Coca-Cola Moves Its Secret Formula to The World of Coca-Cola, Coca-Cola Company, 8 December 2011, available at: <http://www.coca-colacompany.com/press-center/press-releases/coca-cola-moves-its-secret-formula-to-the-world-of-coca-cola#TCCC>. [28 November 2017]

⁵⁵ Chu Huan-Zhang's family has kept formula secret until 1950s, then assigned the formula to Kunming Pharmaceutical company (SOE). Chen, Y 2013, *The Compatibility of Patent Law and Traditional Chinese Medicine*, Ph.D. thesis, HKU, p. 257.

⁵⁶ Many questions in regard to ethnic medicine arise. If they are owned and practiced within an ethnic group does this constitute "public use", or can they still be patented and if so, who is entitled to apply for a patent based on the knowledge. *Ibid.*, p. 146.

⁵⁷ Regulations on the Protection of TCM, promulgated by Decree No. 106 of the State Council of the PRC on 14 October 1992, and effective as of 1 January 1993. Available at:

<http://www.wipo.int/edocs/lexdocs/laws/en/cn/cn336en.pdf>. [28 November 2017]

⁵⁸ *Ibid.*

Article 6 TCM Regulations state the conditions for first class protection: having special curative effects for a certain disease; artificial medicines prepared from varieties of wild medicinal materials analogously under first class protection; or used for the prevention and cure of special diseases. Article 12 TCM Regulations gives the duration of protection for first class protection thirty years, twenty years or ten years and is renewable.

GI

Since it is difficult to protect TCM with patents, the PRC government is encouraging the protection of TCM via GI, and codified this intention explicitly in Article 23 TCM Law.⁵⁹ Of course this is only possible if there is a link between a geographic region, quality, reputation and the medicine. In the PRC, TCM from certain geographical regions can be protected via one or more of the following GI regimes: GI registered by General Administration of Quality, Supervision, Inspection and Quarantine; and the Ministry of Agriculture. The State Administration for Industry and Commerce can protect GI also via collective or certification marks.

4. PROTECTION OF GENETIC MARKERS AND GENOME EDITING TECHNOLOGY VIA IP

Developments in genetics and genomics have made it possible to identify disease susceptibilities, by reading the genome, and ever more possibilities to rewrite the genome and removing the source of the diseases. For these activities AI and its algorithms become ever more important. Trade secrets can help protect algorithms. In addition, patent law can protect genetic markers and genome editing technology.

Genetic markers

In order to know whether a particular person is susceptible to a disease one needs to identify the exact position of a certain gene or genes and the mutations that could cause the disease. Research companies

⁵⁹ *Supra* footnote 1.

invest a lot of funds and time into this process, and therefore they would like to be compensated for their efforts and risk-taking, and harness the protection of the use of the genetic marker via a patent. However, this might impede the flow of information that might spur invention, because researchers need to get a license first to use the patent.

In 1980, in *Diamond v Chakrabarty*, the Supreme Court of the US (SCOTUS) decided that “everything under the sun that man made” can be patented. Therefore, conversely, laws of nature are excluded from patentability.⁶⁰ In 2013, in *Association for Molecular Pathology vs Myriad Genetics*,⁶¹ Myriad Genetics was able to locate human tumor suppressor genes called BRCA1 and BRCA2. Some mutations in these genes increase the chance of breast and ovarian cancer. If these are identified in a person, then preventive measures can be taken.⁶² SCOTUS answered whether isolated fragments of DNA and purified fragments of DNA were protectable via a composition of matter patent.⁶³ The court decided that isolated genomic DNA was not patentable as subject matter, since these parts of the DNA also appear in nature.⁶⁴ However complementary DNA (cDNA) was considered patentable subject matter because here the isolated parts of the DNA were purified by removing the introns (regions of the DNA that do not code for any proteins). According to the SCOTUS, cDNA does not appear in nature.⁶⁵

⁶⁰ *Diamond v Chakrabarty*, 447 U.S. 303 (1980).

⁶¹ *Association for Molecular Pathology v Myriad Genetics*, No. 12-398 (569 U.S. ___ June 13, 2013).

⁶² Payne, E 2013, ‘Angelina Jolie undergoes double mastectomy’, *CNN*, 16 May. Available at:

<http://edition.cnn.com/2013/05/14/showbiz/angelina-jolie-double-mastectomy/index.html>. [28 November 2017]

⁶³ The defense of Myriad Genetics came with an interesting metaphor to claim that an isolated gene sequence does not appear in nature: “a baseball bat doesn’t exist until it’s isolated from a tree.”

⁶⁴ Eric Lander, Professor of Biology at the Massachusetts Institute of Technology, and amicus curiae, confirmed that isolated fragments of fetal DNA can be found in maternal blood including BRCA1 and BRCA2.

Brief for Amicus Curiae in the case *Association for Molecular Pathology v Myriad Genetics, Inc.*, by Eric Lander in support of neither party, No. 12-398, 16, available at:

https://www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-398_neither_amcu_lander.authcheckdam.pdf. [28 November 2017]

⁶⁵ However, Krench points out that cDNA can occur naturally; “certain viruses can copy mRNA to cDNA (in fact, this is where scientists learned the technique).” Krench, M 2013, ‘New Supreme Court Decision Rules That cDNA Is Patentable What It Means for Research and Genetic Testing’, *Scientific American*, 9 July. Available at:

<https://blogs.scientificamerican.com/guest-blog/new-supreme-court-decision-rules-that-cdna-is-patentablewhat-it-means-for-research-and-genetic-testing/>. [28 November 2017]

After two SCOTUS cases; *Mayo Collaborative Services v Prometheus Laboratories, Inc.* in 2012⁶⁶ and *Association for Molecular Pathology v Myriad Genetics* in 2013, modern personalized medicine has become more difficult to protect via patent law in the U.S. After *Mayo* and *Myriad*, Chao and Mapes found out that 22.5% of actions against patent grants were rejected because of patent eligibility problems related to the subject matter, compared with 5.5% in 2011.⁶⁷

Article 5 Patent Law of the PRC points out that those inventions-creations that violate the law, social ethics or harm the public interest, or that rely on genetic resources which are obtained or used in violation of laws or regulations,⁶⁸ cannot be patented. Article 25 Patent Law of the PRC clarifies that scientific discoveries,⁶⁹ rules and methods for intellectual activities⁷⁰ and methods for the diagnosis⁷¹ or treatment of diseases are not eligible as subject matter. In the PRC, gene sequences are granted a scope of protection equivalent to that for ordinary chemical substances.⁷² In contrast to the US, in the PRC isolated genes can be protected via patent protection: a gene or DNA fragment that has been isolated or extracted from nature for the first time is eligible subject matter. The question in the PRC is focused on whether claims for gene patents should be limited to the function or application of the gene sequence or not.⁷³

⁶⁶ In *Mayo Collaborative Services v Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012) SCOTUS decided that claims directed to a diagnostic method for administering a thiopurine drug to patients with autoimmune diseases that involved observing a natural correlation between metabolite levels in the patient's blood and the need to increase or decrease the dosage, were not patent eligible subject matter.

⁶⁷ Chao, B & Mapes, A 2016, 'An Early Look at Mayo's Impact on Personalized Medicine' *U Denver Legal Studies Research Paper No. 16-11*. Available at: <https://ssrn.com/abstract=2758994>. [28 November 2017]

⁶⁸ See also Article 5, *supra* footnote 43: "Patent rights shall not be granted for invention-creations that violate the law or social ethics, or harm public interests. Patent rights shall not be granted for inventions that are accomplished by relying on genetic resources which are obtained or used in violation of the provisions of laws and administrative regulations."

⁶⁹ Article 25(1), *supra* footnote 43.

⁷⁰ *Ibid.*, Article 25(2).

⁷¹ *Ibid.*, Article 25(3).

⁷² Yu, G 2016, 'China v US: what can be patented in the life sciences field?' *LSIPR*, 9 August. Available at: <https://www.lifesciencesipreview.com/article/china-v-us-what-can-be-patented-in-the-life-sciences-field>. [28 November 2017]

⁷³ Wu, L 2015, 'Unique features of China's protection regime for biotechnology patents', *China Business Law Journal*, 7 September. Available at: <https://www.vantageasia.com/unique-features-of-chinas-protection-regime-for-biotechnology-patents/>. [28 November 2017]

Find and Replace

The ultimate prevention of getting ill because of a hereditary disease is to remove the mutations that cause the hereditary disease. CRISPR–Cas9 is a gene editing technology which has revolutionized the process of inserting or deleting bits of DNA into cells, reliably and efficiently.

Combining stem cell technology and CRISPR–Cas9 opens the possibility to remove diseased cells from the body, repair DNA with CRISPR–Cas9 on those cells in the lab and transplant the corrected cells back into the body.⁷⁴

UC Berkeley v Broad Institute, Inc.

On 15 March 2013, Jennifer Doudna at UC Berkeley and Emmanuelle Charpentier, then at University of Vienna, filed a patent application at the USPTO after their research team managed to use CRISPR–Cas9 to edit stretches of bacterial DNA. However, Feng Zhang of the Broad Institute, Inc. of MIT and Harvard, in Cambridge Massachusetts, successfully fast-tracked a patent application at the USPTO for CRISPR–Cas9, demonstrating the use of the gene-editing technique in eukaryotic cells.⁷⁵ The USPTO awarded the Broad Institute the patent for CRISPR–Cas9 in 2014, but not (yet) to UC Berkeley.

UC Berkeley filed a complaint against the decision of the USPTO at the Patent Trial and Appeal Board (PTAB) on 15 February 2017 because of alleged patent interference between the claims in its patent application and Board Institute’s patent. PTAB ruled that the claims of patents granted by the USPTO to Broad Institute, concerning CRISPR editing in eukaryotic cells do not interfere with patent claims filed by UC Berkeley and the University of Vienna: “Specifically, the evidence shows that the invention of such systems in eukaryotic cells would not have been obvious over the invention of CRISPR-Cas9 systems in any environment, including in prokaryotic cells or *in vitro*, because one of ordinary skill in the art would

⁷⁴ Sternberg, S 2016, *What if we could rewrite the human genome?* TEDMED, YouTube video 31 March. Available at: <https://www.youtube.com/watch?v=BSL3k9ezGoA>. [28 November 2017] Doudna, J 2015, *How CRISPR lets us edit our DNA*, TED Talks, YouTube video 12. Available at: <https://www.youtube.com/watch?v=TdBAHexVYzc>. [28 November 2017]

⁷⁵ Eukaryotic cells contain membrane-bound organelles, such as the nucleus, while prokaryotic cells do not.

not have reasonably expected a CRISPR-Cas9 system to be successful in a eukaryotic environment.”⁷⁶ This means that UC Berkeley, if they will get a patent, can assert their right based on the general claim of using CRISPR-Cas9 in all cell environments, but it cannot prevent the Broad Institute’s patent claim related to eukaryotic cells. UC Berkeley has appealed at the Court of Appeals for the Federal Circuit, based in Washington DC.

Of course the battle over CRISPR is not only fought in the US, but also in the PRC. Here the State Intellectual Property Office (Sipo) has given Charpentier’s company CRISPR Therapeutics and Doudna’s two CRISPR startups Intellia and Caribou Biosciences the rights to apply licensing of their CRISPR–Cas9 technology in the PRC.⁷⁷ Sipo recognizes, in contrast to USPTO and PTAB, the broad applicability of their underlying patent applications for uses in all settings, including in human and other eukaryotic cells.

The amount of CRISPR patent families has mushroomed to more than 1,880 families.⁷⁸ And in May 2017, the USPTO issued another “key CRISPR patent” to Vilnius University in Lithuania, because that application was filed earlier than UC Berkeley’s.⁷⁹ Although, the technology has become much easier for researchers, the patent landscape has made it much more complicated to be commercially active in this field as patent holders might assert their rights.

5. CONCLUSIONS

In the philosophy of TCM, preventive medicine is seen as superior to curative medicine. In addition, it is TCM’s goal to solve the root of the disease and not just the symptoms. The protection of TCM via patent law can be difficult if not impossible, because of its often idiosyncratic character and complex ingredients

⁷⁶ *Supra* footnote 40, 2.

⁷⁷ Buhr, S 2017, ‘China sides with Emmanulle Charpentier and Jennifer Doudna in CRISPR patent war’, *TechCrunch*, 19 June. Available at: <https://techcrunch.com/2017/06/19/china-sides-with-emmanulle-charpentier-and-jennifer-doudna-in-crispr-patent-war/>. [28 November 2017]

⁷⁸ Ledford, H 2017, ‘Bitter CRISPR patent war intensifies’, *Nature*, 26 October. Available at: <https://www.nature.com/news/bitter-crispr-patent-war-intensifies-1.22892>. [28 November 2017]

⁷⁹ *Ibid.*

whose prescriptions and formula that are not novel, and whose efficacy are often not recognised by the PHOSITA.

Western evidence-based medicine seems to develop a similar route from fighting downstream symptoms to a more holistic approach taking the genomes of millions of people into account, and develops prescient views on illness using AI, and with gene-editing technology to go after the root of the problem at the DNA level. To protect the genetic markers is complicated by the patent eligibility standards of subject matter. So far, isolated gene fragments can be patented in China, but not in the US. After identification, it is possible to go one step further; remove the root of the problem using CRISPR–Cas9, an efficient and reliant gene-editing technology. Despite its advantages, the crowded patent landscape might make it more difficult for researchers and companies that would like to use this technology, and might slow down the progress of preventive medicine. If there are not sufficient incentives for the medical world to focus on preventive medicine, then the incentives of for example patent law could be recalibrated to be commensurate with the risks. Sir Robin Jacob suggested in such cases a differentiated term of protection and fix the prices for the medicine.⁸⁰

⁸⁰ Friedmann, D 2017, 'Sir Robin Jacob calls for System 2 thinking for patent law', *IP Kat*, 23 November. Available at: <http://ipkitten.blogspot.hk/2017/11/sir-robin-jacob-calls-for-system-2.html>.