

# The March 2018 Newsletter of The GP-TCM Research Association The Easter Holiday & Qingming Festival Special Edition



## Special Features

### **1. The 6<sup>th</sup> Annual Meeting of the Good Practice in Traditional Chinese Medicine Research Association will be held in London, United Kingdom, 4th-6th July 2018.**

The conference will take place at the Royal Botanic Gardens Kew (4th & 5th July 2018) and at London South Bank University (6th July 2018). The conference will bring together scientists, clinicians, regulators and business people involved in different aspects of traditional Chinese medicine (TCM). The conference takes place in the year that celebrates the birth 500 years ago of Li Shizhen. He was the author of the famous Compendium of Materia Medica and considered by many to be the greatest scientific naturalist of China. The aim of the conference is to address the current challenges and opportunities that face the development of TCM as a global resource in modern day medicine.

To reflect our commitments to good practices in TCM research and development, speakers will include representatives from industry that are bringing new medicines to market based on traditional Chinese medicines as well as those studying different aspects of quality control. This will include the need to embrace new techniques and monographs for monitoring the control of granules entering the trade. Other speakers will provide a summary of the increased knowledge about the chemistry, pharmacology and safety of TCM plants and fungi. The first two days of the conference (4th and 5th July) will be at the Royal Botanic Gardens, Kew just outside London. Clinical Studies (herbal) and Acupuncture sessions will be held at London South Bank University (6th July) and will include methodology, evidence, effectiveness, policy and health care provision. The conference will be restricted to about 200 people and there will be no parallel sessions. The conference aims to bring together a multi-disciplinary audience to hear talks from an international group of speakers that will address key questions associated with TCM.

We hope you will be able to attend the conference and share your views as to what needs to be done to optimise the benefits that TCM could contribute to our wellbeing. We will be accepting posters and hope that young scientists will take this opportunity to showcase their findings.

### **Who should attend the conference?**

- Pharmacologists, natural product chemists and those interested in drug development
- Those involved in the conservation and sustainable supply of medicinal plants and fungi
- Companies interested in developing products based on TCM
- Clinicians and acupuncturists involved in TCM

For meeting registration, abstract submission and accommodation, please visit:

<http://www.gp-tcm.org/events/upcoming/>

### **2. Rees M. OBITUARY: Stephen Hawking (1942–2018).**

*Nature* 2018;555:444. World-renowned physicist who defied the odds. When Stephen Hawking was diagnosed with motor-neuron disease at the age of 21, it wasn't clear that he would finish his PhD. Against all expectations, he lived on for 55 years, becoming one of the world's most celebrated scientists... Stephen's expectations when he was diagnosed dropped to zero; he said that everything that had happened since had been a bonus. And what a bonus — for physics, for the millions enlightened by his books and for the even larger number inspired by his achievement against all the odds. [https://www.nature.com/articles/d41586-018-02839-9?WT.ec\\_id](https://www.nature.com/articles/d41586-018-02839-9?WT.ec_id)

The 6th Annual Meeting of  
Good Practice in Traditional Chinese Medicine  
Research Association  
Second Announcement



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**Now Editorial**

## Clinical practice guideline in traditional Chinese medicine: Localization and Globalization



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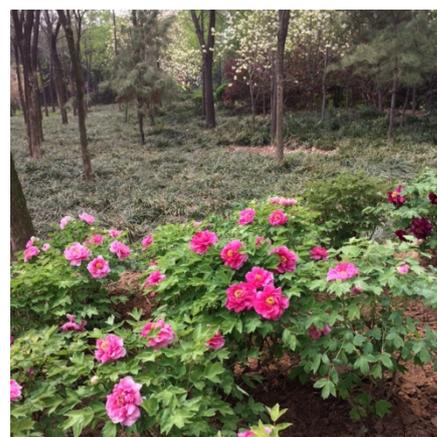
Clinical practice guidelines (CPGs) are classically defined as “systematically developed statements to assist doctors’ and patients’ decisions about appropriate healthcare for specific circumstances”, and are designed to support decision-making processes during patient care [1]. Traditional Chinese medicine (TCM) has been widely practiced in nearly 200 countries and regions while there are few clinical practice guidelines (CPGs) in countries and regions outside mainland China. Most of the TCM treatment schemes worldwide other than mainland China are still based on TCM practitioners’ individual experiences rather than CPGs, which may increase potential risks to patients.

To ensure the safety and quality of TCM practice, Clinical Practice Guidelines on traditional Chinese Medicine (TCM CPG) have been developed in mainland China. The process of developing TCM CPGs began approximately 30 years ago but has accelerated in recent years [2–5]. Until now there were almost 600 TCM CPGs developed by different professional organizations according to routine press briefing of State Administration of Traditional Chinese Medicine of China (SATCM) in 2016. For example, in 2008, the China Association of Chinese Medicine (CATCM) released the ‘Guidelines for Diagnosis and Treatment of Common Internal Diseases in Chinese Medicine [6], which include 132 common internal diseases described by TCM. These guidelines were developed by a national expert panel (comprising more than 200 experts) commissioned by the CATCM. The purpose of these guidelines is to “assist TCM doctors in clinical decision making by describing a range of generally acceptable approaches”. These guidelines are still the most widely used in China [5].

To evaluate the TCM CPG application, a self-administered questionnaire was sent to 4503 TCM practitioners in 28 provinces of China in 2012. The results showed that 85.56% of TCM doctors reported being familiar with CPG recommendations, and most doctors regarded CPG-recommended therapies as safe (92%), economic (84%), and effective (76%) [7]. From this survey, it could be concluded that the majority of TCM doctors support the concept of CPGs for the practice of TCM.

Though TCM CPGs have been developed and widely used in China for many years, there are still some barriers for further promoting the application of TCM CPG worldwide since TCM CPG produced in one regional and/or cultural setting is hardly applied very well in the others. Besides TCM takes emphasis on the individual treatment based on season and regions. Also different regulations, cultural backgrounds and TCM practitioners’ habits would be important factors for TCM CPG development and potential adaption.

To further promote the developed TCM CPG application outside of mainland China, the adaption/re-development process would become a key issue. In the past years, though more high quality of clinical trials have been published, there is still not enough for development of TCM pattern (syndrome, or Zheng) related evidence based CPGs. Started from 2014, supported by Hospital Archives (2008-2018): [www.gp-tcm.org/news-list/](http://www.gp-tcm.org/news-list/)



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Authority in Hong Kong SAR, China, our group was trying to adapt mainland China developed TCM CPGs with good quality for Hong Kong local use. In the development and localization process, AGREE II tools was used to identify the high quality of TCM CPG, and integrated methods, including formal consensus, text mining and evidence-based methods was used for the development of the localized TCM CPG. Considering the TCM practice differences between mainland China and Hong Kong region, the texts were written in traditional Chinese characters instead of simplified ones, and some expressions were modified into conventional Cantonese expressions in order to be consistent with Hong Kong TCM practice. Till now, three TCM CPGs for the treatment of insomnia, cerebral infarction and chronic gastritis were localized in Hong Kong region.



The localization of existed TCM CPGs would give a model for adaption/development of TCM CPGs in other regions and countries. It was known that the guidelines for adapting high quality developed TCM CPG into WHO clinical practice guidelines is under drafting supported by the State Administration of Traditional Chinese Medicine of China.

In coming years, I hope the localization and globalization of mainland China developed TCM CPGs would be conducted more for better taking TCM practice to the world.

## References:

1. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Clinical Practice Guidelines We Can Trust. Port J Nephrol Hypert. 2011.
2. Yuwen Y, Shi NN, Wang LY, Xie YM, Han XJ, Lu AP. Development of clinical practice guidelines in 11 common diseases with Chinese medicine interventions in China. Chinese journal of integrative medicine. 2012, 18(2):112.
3. Tang XD, Zhou LY, Zhan SY, Wang BS. Clinical Practice Guideline of Chinese Medicine for Chronic Gastritis. Chinese journal of integrative medicine. 2012, 18(1):56-71.
4. Zhong LL, Shi NN, Dai L, Ziea TC, Ng B, Tang XD, Bian ZX, Lu AP. Evidence-based chinese medicine clinical practice guideline for stomach pain in Hong Kong. Chinese journal of integrative medicine. 2016:1-8.
5. Wang J, Guo Y, Li GL. Current Status of Standardization of Traditional Chinese Medicine in China. Evidence-based complementary and alternative medicine. 2016, 2016:9123103.
6. China Association of Chinese Medicine. Guidelines for Diagnosis and Treatment of Common Internal Diseases in Chinese Medicine. China Press of Traditional chinese medicine; 2008.
7. Liu M, Zhang C, Zha Q, Yang W, Yuwen Y, Zhong L, Bian Z, Han X, Lu A. A national survey of Chinese medicine doctors and clinical practice guidelines in China. BMC Complement Altern Med. 2017, 17(1):451.

## European Reports

 1. **New booklet on EU research & innovation funding.** The European Commission has published a new booklet showing a few examples where EU support for research and innovation is making a real difference in the lives of citizens and society as a whole. It is aimed at all age groups so everyone can understand the good work EU funding can do.

<http://ec.europa.eu/programmes/horizon2020/en/news/new-booklet-shows-how-eu-research-and-innovation-funding-impacts-your-daily-life?utm>

 2. **UK Position Paper on Framework Programme 9.** The UK Government Department for Business, Energy and Industrial Strategy (BEIS) has today published its position paper on the European Union's ninth Framework Programme for Research and Innovation (FP9). The paper sets out the UK Government's view on how Horizon 2020's successor programme could provide the best economic and social benefits to European citizens as the European Commission begins to develop its

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formal FP9 proposal. Reiterating statements made by the UK Prime Minister, Theresa May, most recently in her speech at Mansion House, the paper highlights the UK's ambition for strong future collaboration with the EU in the area of research and innovation "...through a far-reaching science and innovation pact" allowing for the UK to continue to take part in EU programmes alongside its EU partners with formal options for UK participation in FP9 under consideration.

The paper reflects on the ambition and success of Horizon 2020, including its ability to flexibly respond to new challenges and technologies as evidenced by the Interim Evaluation. Taking into account the recommendations made in the Lamy Report, it suggests that this success could be further strengthened by highlighting and elaborating on nine key components:

- 1) A continued focus on excellence;
- 2) Being open to the world and strengthening international cooperation;
- 3) Adopting a mission-oriented approach determined via a flexible and consultative approach;
- 4) Further simplification and reduction of the administrative burden for participants;
- 5) Spreading excellence and supporting the development of underrepresented groups;
- 6) Ensuring European added value and complementing national programmes;
- 7) Tackling Europe's innovation gap and ensuring industrial competitiveness by exploiting research successes, understanding emerging opportunities, considering the wider industrial landscape and focusing on European added value;
- 8) Demonstrating the impact of its benefits in enhancing growth and providing wider social benefits;
- 9) Rationalising the number of partnership instruments ensuring those that are effective can continue to succeed.

The paper concludes by highlighting the value the UK places on EU Framework Programmes which it again believes should be based around excellence, European added value and impact, noting the importance of building on the existing success of Horizon 2020 rather than introducing drastic change. [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/685997/FP9\\_position\\_paper.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/685997/FP9_position_paper.pdf)

 **3. Innovative Medicines Initiative 2018 Call for Proposals:** The European Commission Directorate-General for Research and Innovation has just launched the Innovative Medicines Initiative (IMI) 2018 Call. The IMI joint undertaking is a public-private partnership (PPP) between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). As part of the H2020 Societal Challenges for Health and Wellbeing, this 2-stage call has an overall estimated budget of €167.2 million. The deadlines for submission of proposals are 14 June and 11 December 2018. Further information on the different topics and the call can be found at the participant Portal, H2020-JTI-IMI-2018.

[http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/calls/h2020-jti-imi2-2018-14-two-stage.html#c\\_topics](http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/calls/h2020-jti-imi2-2018-14-two-stage.html#c_topics)

 **4. EU Council: Consensus Reached on Brexit Withdrawal Agreement.** Good news for UK participation in Horizon 2020 as legal text for withdrawal agreement is agreed by EU 27. While "nothing is agreed until everything is agreed", the legal text now provides a basis for UK participation in EU programmes until the end of the current EU budget period and until the closure of the programmes. The EU27 has also adopted guidelines for the next step of the negotiations and the establishment of a framework for the future relationship between the EU and the UK. The guidelines restate "the Union's determination to have as close as possible a partnership with the UK in the future." but also address potential limitations and various other considerations.



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While "nothing is agreed until everything is agreed", the legal text now provides a basis for UK participation in EU programmes until the end of the current EU budget period and until the closure of the programmes. The EU27 has also adopted guidelines for the next step of the negotiations and the establishment of a framework for the future relationship between the EU and the UK.

There is a short reference in the guidelines on future collaboration in EU programme:"11. In terms of socio-economic cooperation, the following could be envisaged: (...) ii. regarding certain Union programmes, e.g. in the fields of research and

innovation and of education and culture, any participation of the UK should be subject to the relevant conditions for the participation of third countries to be established in the corresponding programmes."

[https://ec.europa.eu/commission/sites/beta-political/files/draft\\_agreement\\_coloured.pdf](https://ec.europa.eu/commission/sites/beta-political/files/draft_agreement_coloured.pdf)

<http://www.consilium.europa.eu/media/33458/23-euco-art50-guidelines.pdf>

**5. Stokstad E. A research behemoth is born in Britain.** *Science* 2018; 359:1319. The United Kingdom has completed a major reorganization of public research funding that brings under one umbrella all the research councils that support U.K. science. The intent is to provide a strategic vision and voice for science, boost efficiency, foster interdisciplinary research, and kick-start an economy jeopardized by Brexit. The new organization, UK Research and Innovation (UKRI), officially opens 1 April. It is headed by Mark Walport, who has led the Wellcome Trust and served as government chief science adviser. One big question is the extent to which UKRI leadership can help bring about a science-friendly outcome for Brexit negotiations, preserving collaborations and funding from Europe. Also unclear is how much autonomy the research councils will keep and whether UKRI will increase the emphasis on biomedical research and the research-intensive southeast. The government has allocated most of £4.7 billion of new science funding to UKRI, ramping up over 4 years, as part of a new industrial strategy. <http://science.sciencemag.org/content/359/6382/1319?utm>

**6. Brexit could be an opportunity for integrating TCM into NHS, says David Tredinnick.**

<https://www.independent.co.uk/news/uk/politics/nhs-chinese-medicine-after-brexit-david-tredinnick-tory-a8269461.html>

## Reports on China and Chinese-European Cooperation

**1. Editorial. Chinese project offers a brighter farming future.** *Nature* 2018;555:141. A massive, decade-long experiment involving millions of Chinese farmers demonstrates an evidence-based approach to sustainability.

[https://www.nature.com/articles/d41586-018-02742-3?WT.ec\\_id](https://www.nature.com/articles/d41586-018-02742-3?WT.ec_id)

**2. New WHO Representative in China - Dr Gauden Galea.**

[https://mp.weixin.qq.com/s/-zKli2\\_Pe62bzaitF2KRjg](https://mp.weixin.qq.com/s/-zKli2_Pe62bzaitF2KRjg) (bilingual: 中文 & English)

**3. Cyranoski D. China tests giant air cleaner to combat smog.** *Nature* 2018;555:152-153. The prototype offers an innovative solution to a major public-health problem.

[http://www.nature.com/articles/d41586-018-02704-9?WT.ec\\_id](http://www.nature.com/articles/d41586-018-02704-9?WT.ec_id)

**4. Cyranoski D. Chinese leaders create grand science ministry.** *Nature* 2018;555:425. Chinese leaders released plans last week to expand the powers of the country's science and technology ministry (MOST). The beefed-up agency will continue to oversee science policy and major projects, but will take on extra responsibilities for funding research grants and for recruiting foreign scientists. Politicians say that the reforms will streamline government procedures, but some science-policy experts warn that the changes could weaken support for basic research.

[https://www.nature.com/articles/d41586-018-03246-w?WT.ec\\_id](https://www.nature.com/articles/d41586-018-03246-w?WT.ec_id)

**5. A "Two Sessions" Summary on China's Medical and Pharmaceutical industry in 2018.**

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[https://mp.weixin.qq.com/s/Dtl\\_90k\\_wX0D484ypBcl7Q](https://mp.weixin.qq.com/s/Dtl_90k_wX0D484ypBcl7Q) (中文)

**6. Tackling drug resistance: UK-China funding competition opens.** A competition has opened that will make up to £10 million available to UK academic and industrial organisations to work in a consortium with Chinese partners.  
<https://www.gov.uk/government/news/tackling-drug-resistance-uk-china-funding-competition-opens>

**7. Ministry of Science & Technology international funds 2018** (incl. TCM & acupuncture)  
[http://www.most.gov.cn/mostinfo/xinxifenlei/fgzc/gfxwj/gfxwj2018/201803/t20180326\\_138789.htm](http://www.most.gov.cn/mostinfo/xinxifenlei/fgzc/gfxwj/gfxwj2018/201803/t20180326_138789.htm)

**8. China's Big Science & Big Engineering Initiative** (incl. TCM & acupuncture)  
<https://mp.weixin.qq.com/s/W2Sudhn0KZ8GuvrKURvUYg> (中文)

## TCM, Acupuncture and Other Traditional Medicine

**1. Wang S et al. The status quo and outlook of the ginseng industry.** *Modern Chinese Medicine* 2016;18:3-6. Ginseng industry involves the synchronous development of a lot of fields in the primary · secondary and tertiary industries. It is a typical and representative case in the Chinese herbal medicine industry development. This paper gives a brief description and analysis of the development of ginseng industry in China · and put forward the basic thoughts on the scientific and technological innovation of ginseng industry. The industrialization progress experience plays an important role not only in the development of other large varieties of Chinese medicinal materials but also in the exploration on the system of traditional Chinese medicine.  
<http://mp.weixin.qq.com/s/tsYHtOHnw53TOxGRu3Pshg> (中文)

**2. Tasting TCM drugs by bionic technology**  
<http://mp.weixin.qq.com/s/9ewuflKkTfWT3tsWYVMAJg> (中文)

**3. An illustrated overview of the proprietary TCM drug market**  
[http://mp.weixin.qq.com/s/En98Xt\\_jF3CNSD9Yc\\_SzjA](http://mp.weixin.qq.com/s/En98Xt_jF3CNSD9Yc_SzjA) (中文)

**4. Zare R, et al. RCT: Efficacy of Cinnamon in Patients with Type II Diabetes Mellitus.** *Clin Nutrition* 2018; in press. Based on the study findings, cinnamon may improve anthropometric parameters, glycemic indices and lipid profile of patients with type II diabetes. These benefits are significantly more prominent in patients with higher baseline BMI (BMI ≥ 27)...  
<https://www.sciencedirect.com/science/article/pii/S0261561418301146>

**5. Xu J, et al. Structural modulation of gut microbiota during alleviation of type 2 diabetes with a Chinese herbal formula.** *ISME J.* 2015;9:552-62.  
<https://www.ncbi.nlm.nih.gov/pubmed/25279787>

**6. TCM monotherapies: 60 TCM therapies using a single traditional medicinal material**  
<http://mp.weixin.qq.com/s/ONylaE-JqE9SStcgiSzA6g> (中文)

**7. Totality quality control of TCM standardized decoctions**  
[https://mp.weixin.qq.com/s/qBPIsBbscFZMY4\\_ehF58uw](https://mp.weixin.qq.com/s/qBPIsBbscFZMY4_ehF58uw) (中文)



## Omics in Progress

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**Now** 1. Ge S, et al. **A proteomic landscape of diffuse-type gastric cancer.** *Nat Commun.* 2018;9:1012. The diffuse-type gastric cancer (DGC) is a subtype of gastric cancer with the worst prognosis and few treatment options. Here we present a dataset from 84 DGC patients, composed of a proteome of 11,340 gene products and mutation information of 274 cancer driver genes covering paired tumor and nearby tissue. DGC can be classified into three subtypes (PX1-3) based on the altered proteome alone. PX1 and PX2 exhibit dysregulation in the cell cycle and PX2 features an additional EMT process; PX3 is enriched in immune response proteins, has the worst survival, and is insensitive to chemotherapy. Data analysis revealed four major vulnerabilities in DGC that may be targeted for treatment, and allowed the nomination of potential immunotherapy targets for DGC patients, particularly for those in PX3. This dataset provides a rich resource for information and knowledge mining toward altered signaling pathways in DGC and demonstrates the benefit of proteomic analysis in cancer molecular subtyping.



<http://www.nature.com/articles/s41467-018-03121-2>  
<http://www.chinanews.com/m/jk/2018/03-08/8463274.shtml> (中文)

**Now** 2. Gröbner SN, et al. **The landscape of genomic alterations across childhood cancers**

*Nature* 2018;555:321–327. Pan-cancer analyses that examine commonalities and differences among various cancer types have emerged as a powerful way to obtain novel insights into cancer biology. Here we present a comprehensive analysis of genetic alterations in a pan-cancer cohort including 961 tumours from children, adolescents, and young adults, comprising 24 distinct molecular types of cancer. Using a standardized workflow, we identified marked differences in terms of mutation frequency and significantly mutated genes in comparison to previously analysed adult cancers. Genetic alterations in 149 putative cancer driver genes separate the tumours into two classes: small mutation and structural/copy-number variant (correlating with germline variants). Structural variants, hyperdiploidy, and chromothripsis are linked to TP53 mutation status and mutational signatures. Our data suggest that 7–8% of the children in this cohort carry an unambiguous predisposing germline variant and that nearly 50% of paediatric neoplasms harbour a potentially druggable event, which is highly relevant for the design of future clinical trials.

[https://www.nature.com/articles/nature25480?WT.ec\\_id](https://www.nature.com/articles/nature25480?WT.ec_id)

**Now** 3. Ma X et al. **Pan-cancer genome and transcriptome analyses of 1,699 paediatric leukaemias and solid tumours.** *Nature* 2018;555:371–376. Analysis of molecular aberrations across multiple cancer types, known as pan-cancer analysis, identifies commonalities and differences in key biological processes that are dysregulated in cancer cells from diverse lineages. Pan-cancer analyses have been performed for adult but not paediatric cancers, which commonly occur in developing mesodermic rather than adult epithelial tissues. Here we present a pan-cancer study of somatic alterations, including single nucleotide variants, small insertions or deletions, structural variations, copy number alterations, gene fusions and internal tandem duplications in 1,699 paediatric leukaemias and solid tumours across six histotypes, with whole-genome, whole-exome and transcriptome sequencing data processed under a uniform analytical framework. We report 142 driver genes in paediatric cancers, of which only 45% match those found in adult pan-cancer studies; copy number alterations and structural variants constituted the majority (62%) of events. Eleven genome-wide mutational signatures were identified, including one attributed to ultraviolet-light exposure in eight aneuploid leukaemias. Transcription of the mutant allele was detectable for 34% of protein-coding mutations, and 20% exhibited allele-specific expression. These data provide a comprehensive genomic architecture for paediatric cancers and emphasize the need for paediatric cancer-specific development of precision therapies.

[https://www.nature.com/articles/nature25795?WT.ec\\_id](https://www.nature.com/articles/nature25795?WT.ec_id)

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**4. Mure LS et al. Diurnal transcriptome atlas of a primate across major neural and peripheral tissues. *Science* 2018;359:eaao0318**

**INTRODUCTION:** The interaction among cell-autonomous circadian oscillators—daily cycles of activity–rest and feeding–fasting—produces diurnal rhythms in gene expression in almost all animal tissues. These rhythms control the timing of a wide range of functions across different organs and brain regions, affording optimal fitness. Chronic disruption of these rhythms predisposes to and are hallmarks of numerous diseases and affective disorders.

**RATIONALE:** Time-series gene expression studies in a limited number of tissues from rodents have shown that 10 to 40% of the genome exhibits a ~24-hour rhythm in expression in a tissue-specific manner. However, rhythmic expression data from diverse tissues and brain regions from humans or our closest primate relatives is rare. Such multitissue diurnal gene expression data are necessary for gaining mechanistic understanding of how spatiotemporal orchestration of gene expression maintains normal physiology and behavior. We used a RNA sequencing technique to assess gene expression in major tissues and brain regions from baboons (a primate closely related to humans) housed under a defined 24-hour light–dark and feeding–fasting schedule.

**RESULTS:** We assessed gene expression in 64 different tissues and brain regions of male baboons, collected every 2 hours over the 24-hour day. Tissue-specific transcriptomes in baboon were comparable with that from humans (Human GTEx data set). We detected >25,000 expressed transcripts, including protein-coding and -noncoding RNAs. Nearly 11,000 genes were commonly expressed in all tissues. These universally expressed genes (UEGs) encoded for basic cellular functions such as transcription, RNA processing, DNA repair, protein homeostasis, and cellular metabolism. The remainders were expressed in distinct sets of tissues, with ~1500 genes expressed exclusively in a single tissue. Rhythmic transcripts were found in all tissues, but the number of cycling transcripts varied from ~200 to >3000 in a given tissue, with only limited overlap in the repertoire of rhythmic transcripts between tissues. Of the 11,000 UEGs, the vast majority (96.6%) showed 24-hour rhythmicity in at least one tissue. A majority (>80%) of the 18,000 protein-coding genes detected also exhibited 24-hour rhythms in expression. The most enriched rhythmic transcripts across tissues were core clock components and their immediate output targets. However, their relative abundance and robustness of daily rhythms varied across tissues. Considered at the organismal level, global rhythmic transcription in 64 tissues organized into bursts of peak transcription, during early morning and late afternoon (when 11,000 transcripts reach their peak level). By contrast, during a relative “quiescent phase” in early evening that coincides with the onset of sleep and no food intake, only 700 rhythmic transcripts reach their peak expression level.



**CONCLUSION:** The daily expression rhythms in >80% of protein-coding genes, encoding diverse biochemical and cellular functions, constitutes by far the largest regulatory mechanism that integrates diverse biochemical functions within and across cell types. From a translational point of view, rhythmicity may have a major impact in health because 82.2% of genes coding for proteins that are identified as druggable targets by the U.S. Food and Drug Administration show cyclic changes in transcription.

<http://science.sciencemag.org/content/359/6381/eaao0318?utm>

**5. Jessica Sheu-Gruttadauria, Ian J. MacRae. Phase Transitions in the Assembly and Function of Human miRISC. *Cell* 2018; in press.** miRISC is a multi-protein assembly that uses microRNAs (miRNAs) to identify mRNAs targeted for repression. Dozens of miRISC-associated proteins have been identified, and interactions between many factors have been examined in detail. However, the physical nature of the complex remains unknown. Here, we show that two

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core protein components of human miRISC, Argonaute2 (Ago2) and TNRC6B, condense into phase-separated droplets in vitro and in live cells. Phase separation is promoted by multivalent interactions between the glycine/tryptophan (GW)-rich domain of TNRC6B and three evenly spaced tryptophan-binding pockets in the Ago2 PIWI domain. miRISC droplets formed in vitro recruit deadenylation factors and sequester target RNAs from the bulk solution. The condensation of miRISC is accompanied by accelerated deadenylation of target RNAs bound to Ago2. The combined results may explain how miRISC silences mRNAs of varying size and structure and provide experimental evidence that protein-mediated phase separation can facilitate an RNA processing reaction.



[http://www.cell.com/cell/fulltext/S0092-8674\(18\)30228-9](http://www.cell.com/cell/fulltext/S0092-8674(18)30228-9)

**6. Bedrosian TA et al. Early life experience drives structural variation of neural genomes in mice** *Science* doi:10.1126/science.aah3378, 2018. **Mouse Moms' Behavior Affects Pups' Genome Structures:** Mice who get less attention from their mothers have more copies of a common retrotransposon in the genomes of their hippocampal neurons. Some mouse mothers groom, lick, and nurse their babies more than others. In a study published in *Science* on March 23, researchers demonstrate that this natural variation in maternal behavior is linked to the structure of pups' genomes, specifically, the activation of one of the most common jumping genes in the genome, LINE-1. "What's fascinating about the paper is the connection between experience, epigenetics, and restructuring of the genome," says Moshe Szyf, a geneticist at McGill University in Montreal who did not participate in the work. "We usually think about epigenetics changes that don't change the sequence, but here there was a connection of the maternal care, the change in methylation . . . and then restructuring."

<http://science.sciencemag.org/content/359/6382/1395>

<https://www.the-scientist.com/?articles.view/articleNo/52124/title/Mouse-Moms--Behavior-Affects-Pups--Genome-Structures/&utm>

**7. Svensson V, Vento-Tormo R, Teichmann SA. Exponential scaling of single-cell RNA-seq in the past.** *Nature Protocols* 2018;13:599-604. Here Sarah Teichmann and colleagues provide a Perspective on the exponential scaling of single-cell RNA-sequencing experiments over the last decade, commenting on the methodological developments that have underpinned the advances in this technology. [https://www.nature.com/articles/nprot.2017.149?WT.ec\\_id](https://www.nature.com/articles/nprot.2017.149?WT.ec_id)

**8. Forsberg EM et al. Data processing, multi-omic pathway mapping, and metabolite activity analysis using XCMS Online.** *Nature Protocols* 2018;13:633-651. This protocol describes XCMS Online, a web-based systems biology platform for processing of metabolomics data, pathway mapping and integration with genomics and proteomics data. [https://www.nature.com/articles/nprot.2017.151?WT.ec\\_id](https://www.nature.com/articles/nprot.2017.151?WT.ec_id)

**9. Livigni A, et al. A graphical and computational modeling platform for biological pathways.** *Nature Protocols* 2018;13:705-722. A major endeavor of systems biology is the construction of graphical and computational models of biological pathways as a means to better understand their structure and function. Here, we present a protocol for a biologist-friendly graphical modeling scheme that facilitates the construction of detailed network diagrams, summarizing the components of a biological pathway (such as proteins and biochemicals) and illustrating how they interact. These diagrams can then be used to simulate activity flow through a pathway, thereby modeling its dynamic behavior. The protocol is divided into four sections: (i) assembly of network diagrams using the modified Edinburgh Pathway Notation (mEPN) scheme and yEd network editing software with pathway information obtained from published literature and databases of molecular interaction data; (ii) parameterization of the pathway model within yEd through the placement of 'tokens' on the basis of the known or imputed amount or activity of a

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component; (iii) model testing through visualization and quantitative analysis of the movement of tokens through the pathway, using the network analysis tool Graphia Professional and (iv) optimization of model parameterization and experimentation. This is the first modeling approach that combines a sophisticated notation scheme for depicting biological events at the molecular level with a Petri net–based flow simulation algorithm and a powerful visualization engine with which to observe the dynamics of the system being modeled. Unlike many mathematical approaches to modeling pathways, it does not require the construction of a series of equations or rate constants for model parameterization. Depending on a model's complexity and the availability of information, its construction can take days to months, and, with refinement, possibly years. However, once assembled and parameterized, a simulation run, even on a large model, typically takes only seconds. Models constructed using this approach provide a means of knowledge management, information exchange and, through the computation simulation of their dynamic activity, generation and testing of hypotheses, as well as prediction of a system's behavior when perturbed. <http://www.nature.com/articles/nprot.2017.144>

## Other Recommended Readings

 1. **Nature Key Advances in Medicine January 2018.** Much like our oceans, the world of clinical and biomedical research is vast, fast-paced, dynamic and full of unanswered questions. In 2017, numerous advances were made *that could change the tide of efforts to fight disease*. The **Key Advances in Medicine eBook** distills the major discoveries made in 2017 and highlights trends to look out for in 2018. This eBook is free to access and download, and contains 44 articles written by international experts who have identified the top ground-breaking papers published within their specialties. Altogether, the authors provide summaries and critiques of >200 key papers published in leading journals. *Key Advances in Medicine*, a product from the eight clinical *Nature Reviews* journals, is a vital resource for busy students, physicians and clinical researchers who want expert opinion on the most important developments in 2017.



<https://www.nature.com/collections/gvzvzmcfrv>  
<http://s3-service-broker-live-19ea8b98-4d41-4cb4-be4c-d68f4963b7dd.s3.amazonaws.com/uploads/ckeditor/attachments/8816/KAiM-jan18.pdf>

 2. Gewin V. **How to write a first-class paper.** *Nature* 2018;**555**:129-130. Manuscripts may have a rigidly defined structure, but there's still room to tell a compelling story — one that clearly communicates the science and is a pleasure to read. Scientist-authors and editors debate the importance and meaning of creativity and offer tips on how to write a top paper.

- Think about the message you want to give to readers. If that is not clear, misinterpretations may arise later.
- Structure is paramount. If you don't get the structure right, you have no hope.
- In each paragraph, the first sentence defines the context, the body contains the new idea and the final sentence offers a conclusion. For the whole paper, the introduction sets the context, the results present the content and the discussion brings home the conclusion.
- It's crucial to focus your paper on a single key message, which you communicate in the title. Everything in the paper should logically and structurally support that idea. It can be a delight to creatively bend the rules, but you need to know them first.
- You have to guide the naive reader to the point at which they are ready to absorb what you did. As a writer, you need to detail the problem. I won't know why I should care about your experiment until you tell me why I should.
- Clarity is the sole obligation of the science writer, yet I find constantly that the 'What's new' element is buried. Answering one central question — What did you do? — is the key to finding

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the structure of a piece. Every section of the manuscript needs to support that one fundamental idea.

- Always think of your busy, tired reader when you write your paper — and try to deliver a paper that you would enjoy reading yourself.
- Scientific writing should be factual, concise and evidence-based, but that doesn't mean it can't also be creative — told in a voice that is original — and engaging.

<https://www.nature.com/articles/d41586-018-02404-4>

<https://www.elsevier.com/connect/writing-a-science-paper-some-dos-and-donts>

<http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1005619>

[http://www.cell.com/trends/ecology-evolution/fulltext/S0169-5347\(17\)30159-3](http://www.cell.com/trends/ecology-evolution/fulltext/S0169-5347(17)30159-3)

<https://www.sciencedirect.com/science/article/pii/S0169534717301593?via%3Dihub>

**3. Best of Trends in 2017.** *Cell Press* have been publishing reviews that are a concise synthesis of important topics, authored by experts in the field, spanning the life sciences. We wanted to use this same curation strategy to share the best of the best, and the reviews that inspired us in 2017. Every editor and reader may have different criteria for what he or she may consider is the "best" review, and likewise each editor also took their own approach to this question. Some used download and citation data, some thought about the impact of the research on society, and others decided to feature a topic that they felt was especially timely and relevant for their field.

<http://crosstalk.cell.com/blog/topic/best-of-trends?utm>

**4. Gurevitch J, et al. Meta-analysis and the science of research synthesis.** *Nature* 2018; 555:175–182. Meta-analysis—the quantitative, scientific synthesis of research results—has been both revolutionary and controversial, with rapid advances and broad implementation resulting in substantial scientific advances, but not without pitfalls...

[https://www.nature.com/articles/nature25753?WT.ec\\_id](https://www.nature.com/articles/nature25753?WT.ec_id)

**5. Zhao L, et al. Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes.** *Science* 2018;359: 1151-1156. Short-chain fatty acids (SCFAs) are produced by various human gut microbes. SCFAs act as an energy source to the colonic epithelium and are also sensed by host signaling pathways that modulate appetite and inflammation. Deficiency of gut SCFAs is associated with type 2 diabetes. Zhao et al. found that adopting a high-fiber diet promoted the growth of SCFA-producing organisms in diabetic humans. The high-fiber diet induced changes in the entire gut microbe community and correlated with elevated levels of glucagon-like peptide-1, a decline in acetylated hemoglobin levels, and improved blood-glucose regulation.

<http://science.sciencemag.org/content/359/6380/1151>

**6. Daley J. Want to Boost Reproducibility? Get Another Lab Involved.** *The Scientist* 22 Feb. 2018. Including as few as two labs in a study improved the odds of getting the true effect size by as much as 23 percentage points, according to a replication model.

<https://www.the-scientist.com/?articles.view/articleNo/51879/title/Want-to-Boost-Reproducibility--Get-Another-Lab-Involved/>

**7. Lucan SC. When food isn't medicine - A challenge for physicians and health systems.** *Preventive Medicine Reports.* 2018; 10:62-65. Food can be powerful medicine. Good nutrition helps promote health and prevent and treat disease. Yet nutrition is not often part of a physician's training or clinical practice. Food might not be medicine when it's importance is under-recognized and healthful eating is under-prescribed. Moreover, food cannot be medicine when it is not available to patients (or when available only in the form of unhealthful fare). This paper considers evolving thinking about



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when food isn't medicine by chronicling the experience of one physician—from college coursework to providing patient care and conducting research. The paper is framed around the experience of a representative patient struggling with diet-related chronic conditions, and describes some community-focused initiatives to help address issues related to food access in challenged communities. A principal focus is the overabundance of foods from 'plants' (the industrial processing kind) and the low availability of food from 'plants' (the living botanical kind). Physicians and health systems can support access to healthier food and healthier eating, and the idea of food as medicine, through a variety of approaches that extend beyond hospital and clinic walls. Examples of such physician and health-system approaches are provided.



<https://www.sciencedirect.com/science/article/pii/S2211335518300251>

**8. Statistical errors may taint as many as half of mouse studies.**

<https://spectrumnews.org/news/statistical-errors-may-taint-many-half-mouse-studies/Future>

**9. Ioannidis JPA. The Proposal to Lower *P* Value Thresholds to .005. *JAMA*. Published online March 22, 2018. doi:10.1001/jama.2018.1536.**

<https://jamanetwork.com/journals/jama/fullarticle/2676503>

**10. The most cited review in the history of *Cell* updated. It's an update on microRNAs.** The paper is Bartel DP. **Metazoan MicroRNAs.** *Cell* 2018;173:20-51. In 2004, David Bartel published a review in *Cell* on microRNAs, small but powerful molecules that play widespread roles in gene regulation. Over the past 14 years, that paper has become the most cited review in the history of *Cell*. On 22<sup>nd</sup> March 2018, Dr. Bartel has updated his review to reflect the latest advances in this field, including how microRNAs recognize their targets, how they perform their biological functions, and how they impact development, physiology, and disease.

**Why is this review so important now?** “Since the abundance of microRNAs was discovered in 2001, there's been a surge in interest in these regulatory RNAs. I have updated the first review because since it was written, we've learned a lot about how microRNAs work and what they do — both molecularly, when they recognize and repress their targets, and biologically, when they influence the development or physiology of the animal. We now know that microRNAs regulate the mRNAs of most human genes. We also know that most of the highly conserved microRNAs in flies, in mice, and, presumably, in humans play important roles in development or physiology. After compiling all the work that's been done examining knockout phenotypes, it's very interesting to see how many different developmental processes and diseases they can impact.” Dr. David Bartel is a member of the Whitehead Institute for Biomedical Research, a professor at the Massachusetts Institute of Technology, and a Howard Hughes Medical Institute investigator.

[http://www.cell.com/cell/fulltext/S0092-8674\(18\)30286-1](http://www.cell.com/cell/fulltext/S0092-8674(18)30286-1)

**11. The Secret to a Longer Life? Don't Ask These Dead Longevity Researchers.**

<https://www.nytimes.com/2018/03/09/opinion/sunday/longevity-pritikin-atkins.html>

**12. 2018 and Beyond: Outlook and Turning Points.** This report describes ten predicted changes that will impact global health in 2018 and beyond and highlights impactful areas where stakeholders are using evidence and technology to solve the problems of human health. This report focuses on facts and data, and attempts to bring evidence to topics often hotly debated and discussed in the public realm. Key themes include trends in innovation, technology and healthcare spending.

**Report Summary:** Global health is poised to meet a series of key turning points, and changes seen in 2018 will mark the key inflections that drive the outlook for the next five years and beyond. The types of medicines being developed, the way technology contributes to health, and how the value of healthcare is calculated are all markedly changing.

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Innovation is a key theme, including the way regulators of medicine and applicants filing for approval will increasingly support clinical submissions with real world data. A wave of cell and gene therapies are bending the definition of what constitutes a drug, both clinically, and in terms of expectations of outcomes, duration of treatment and costs.

Technology itself can be a treatment, and mobile apps are newly appearing in treatment guidelines as a key feature of future care paradigms. Furthermore, mobile technology can be an enabler of telehealth communication that brings providers and patients together at substantially lower costs than traditional consultations.

In recent years, concerns about escalating medicine costs have captured significant attention. In 2018, some of the key drivers of medicine spending growth appear to be slowing spending rather than driving it upward. The causes of slowing growth are directly linked to payers concerns about budgets and to newly emerging mechanisms to adjudicate value and thus limit the potential for out-of-control spending growth.



<https://www.iqvia.com/es-es/institute/reports/2018-and-beyond-outlook-and-turning-points>

<http://mp.weixin.qq.com/s/-RjYn8nb6Zh3q4HAlubWtA> (中文)

**13. Benias PC, et al. Structure and Distribution of an Unrecognized Interstitium in Human Tissues.** *Scientific Reports*, 2018; 8 (1) DOI: 10.1038/s41598-018-23062-6

<https://www.nature.com/articles/s41598-018-23062-6>

[http://www.science20.com/news\\_staff/interstitium\\_newfound\\_organ\\_missed\\_due\\_to\\_old\\_standard\\_method\\_for\\_visualizing\\_anatomy-231415](http://www.science20.com/news_staff/interstitium_newfound_organ_missed_due_to_old_standard_method_for_visualizing_anatomy-231415)

<https://mp.weixin.qq.com/s/peJcWYP4ShVBYsTUv6iEKq> (中文)

<http://mp.weixin.qq.com/s/k2V1ZODUs0ab8k3mZegULA> (中文)

**14. Dance A. Why laughter in the lab can help your science.** *Nature* 2018; 555:689-691. Science is serious business, but as April Fool's Day looms, a judicious prank can lighten up life in the lab.

<https://www.nature.com/articles/d41586-018-03802-4>

## Meetings & Events

**1. The Third Natural Medicine Conference & Hong Kong-Macao-Taiwan Forum 2018.** Chaired by Professor Hongxin Xu, Dean, School of Pharmacy, Shanghai University of TCM, the meeting will be held in Shanghai on 12-13<sup>th</sup> April.

<https://s.wcd.im/v/134lcZav/?slv=3&sid=4v0c&from=groupmessage&isappinstalled=0> (中文)

**2. The 6<sup>th</sup> Annual Meeting of the GP-TCM Research Association will be held at Royal Botanic Gardens, Kew, UK on 4-6 July 2018.** Please refer to Special Features in page 2.

**3. TROPHARM seminar Pharmaceutical opportunities in DR Congo / BE: an interdisciplinary approach,** Faculty of Pharmaceutical Sciences, Campus Heymans, Ottergemsesteenweg 460, 9000 Ghent, THURSDAY 17 MAY 2018 | 13:30-16:30, followed by Reception and network event ,16:30.

- Experience and management in the domain of sickle cell disease or sickle cell anemia
- Traditional foods as putative nutraceuticals in Konzo
- Use of traditional drugs in obstetrics
- Quality and safety of food consumed in DR Congo

Introductory talks by deans Prof. José Lami and Prof. Jan Van Bocxlaer. Notes by professors of University of Kinshasa, DRC: Prof. Christophe Masiala, Prof. Dr. Roger Mbungu, Prof. Pius Mpiana and Prof. Nadege Ngombe.

MORE INFORMATION: [ciska.deruyver@ugent.be](mailto:ciska.deruyver@ugent.be)

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REGISTER BEFORE 15th MAY 2018 at

<https://webappsx.ugent.be/eventManager/events/TROPHARMseminar>

4. **International celebration of the 500 anniversary of Li Shizhen's birth to be held in Li's hometown Jichun County, Hubei Province, China, on 26th May, 2018.**

<http://mp.weixin.qq.com/s?biz=MzAxMjMyMTEwNA==&mid=2660692447&idx=1&sn=3895e03e994d2f1c98befd9f4beb8eca&chksm>

(中文)

5. **The 17th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Kuching-Sarawak, Malaysia on August 8 - 10, 2018.** This year's meeting is going to

be organized by the Malaysian Institute of Pharmaceuticals and Nutraceuticals, National Institutes of Biotechnology Malaysia. The meeting provides a platform for regulatory-industrial-academic exchanges and potential research collaborations, on various frontiers of Traditional Chinese Medicine among our worldwide CGCM members and guests. You are cordially invited to attend the meetings and submit abstracts. Preliminary programme and more details will soon be announced on our website. Should you have any enquiries, please feel free to contact the CGCM Central Office:

Email: [centraloffice@tcmedicine.org](mailto:centraloffice@tcmedicine.org); Website: [www.tcmedicine.org](http://www.tcmedicine.org)

**Information for meeting program, abstract submission, registration and travel grant can be found here:** <http://www.cgcm2018.com>

**Important dates:**

- **May 31, 2018** Early Bird Registration
- **July 16, 2018** Registration Deadline
- **May 31, 2018** Abstract Submission Deadline
- **June 15, 2018** Travel grant application deadline

6. **The 15th World Congress of Chinese Medicine and Belt and Road TCM Culture Week to be held in Rome, Italy, 16-20 November 2018.**

[http://c.eqxiu.com/s/O8xAcE2w?eqrcode=1&share\\_level=4&from\\_user=a294a700-73b5-4d95-9d8b-dc428813e7cd&from\\_id](http://c.eqxiu.com/s/O8xAcE2w?eqrcode=1&share_level=4&from_user=a294a700-73b5-4d95-9d8b-dc428813e7cd&from_id) (中文)

<http://mp.weixin.qq.com/s/R5Ao3tYI7Q2UwzaP94ikTw> (中文)

7. Xuetao Cao, Helena Hui Wang, Limin Li, William Summerskill, Richard Horton. **The Lancet-CAMS Health Summit 2018: a call for abstracts.** *Lancet* 2018;391:188-9. Please submit your abstract as a Word document through The Lancet's online submission system **no later than May 31, 2018**, stating in your covering letter that the submission is in response to this call for abstracts from China. Please note, abstracts submitted later than May 31 will not be considered.

<https://ees.elsevier.com/thelancet/default.asp?pg=login.asp>

## Invitation from WJTCM

1. **World Journal of Traditional Chinese Medicine: Sincere invitation for submissions.**

World Journal of Traditional Chinese Medicine (ISSN 2311-8571, CN10-1395/R) is sponsored by WFCMS, and is the official journal of GP-TCM RA. WJTCM dedicates to report the research progress in clinical efficacy and action mechanism of Traditional Chinese Medicine, Chinese materia medica, acupuncture and moxibustion to doctors

Archives (2008-2018): [www.gp-tcm.org/news-list/](http://www.gp-tcm.org/news-list/)



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and biomedical researchers around the world, so as to provide new thoughts and methods for solving complex diseases and knotty diseases. To submit your manuscripts, or to read articles in the past issues, please visit: <http://www.wjtcn.net>

**2. *Frontiers in Pharmacology* special issue “Can Natural Products Reduce the Side Effects of Cancer Therapies?” invites your submission.** Deadline: June 2018.  
<https://www.frontiersin.org/research-topics/7625/can-natural-products-reduce-the-side-effects-of-cancer-therapies>  
<http://journal.frontiersin.org/researchtopic/7625> (中文)

## Sounding Board

This column is reserved for comments, personal views, proposals for collaborations or any other features from our readers across the world. We look forward to hearing from you! Please get in touch with your editors: Dr Qihe Xu ([qihe.xu@kcl.ac.uk](mailto:qihe.xu@kcl.ac.uk)), Prof. Pierre Duez ([pierre.duez@umons.ac.be](mailto:pierre.duez@umons.ac.be)) and Prof. Yuan Shiun Chang ([yschang0404@gmail.com](mailto:yschang0404@gmail.com)).

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