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A single nucleotide distinguishes the SARS-CoV-2 in the Wuhan outbreak in December 2019 from that in Beijing-Xinfadi in June 2020, China

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Abstract

Two major locally transmitted outbreaks of coronavirus disease 2019 occurred in China, one in Wuhan from December 2019 to April 2020, another in Beijing-Xinfadi in June 2020. Severe acute respiratory syndrome coronavirus 2 isolated from these two outbreaks can be distinguished by a conserved pyrimidine nucleotide located at nucleotide position 241 in the 5'-untranslated region of the virus genome.

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Coronavirus disease 2019 (COVID-19), an ongoing pandemic, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Like SARS-CoV-1, which caused the 2002–2004 SARS outbreak [2], SARS-CoV-2 is also a member of the genus β-coronavirus [3]. The genome of SARS-CoV-2 is a positive-sense, single-stranded RNA that is ~29.8 kb in length and possesses 14 open reading frames [4].

COVID-19 was first identified in December 2019 in Wuhan, Hubei province of China [5,6]. The rapid local transmission of SARS-CoV-2 resulted in the lockdown of Wuhan city from 23 January until 8 April 2020. On 11 June 2020, after 55 days without a locally transmitted COVID-19 case, another metropolitan area, Beijing, the capital of China, reported the first COVID-19 case [7]. By 19 June 2020, 205 cases were officially confirmed and most of these patients went to Beijing-Xinfadi wholesale market. This second outbreak of locally transmitted COVID-19 in Beijing-Xinfadi led to a partial lockdown of Beijing.

On 17 June 2020, three complete genomic sequences of the SARS-CoV-2 isolated in Beijing-Xinfadi were available on the GISAID initiative database (https://www.gisaid.org). We compared these newly identified viral sequences with that isolated from the first locally transmitted COVID-19 outbreak in Wuhan and found a uniquely conserved pyrimidine nucleotide located at nucleotide position 241 relative to the SARS-CoV-2 reference sequence (NCBI reference no. NC_045512.2) (Fig. 1a). This conserved pyrimidine nucleotide is located in the loop region of stem-loop 5B (SL5B) [8] of the 5'-untranslated region of the virus genome (Fig. 1b) and can be used to distinguish the virus in Beijing-Xinfadi from that in Wuhan. Viruses isolated from both the environment and the patients in Beijing-Xinfadi have a uridine nucleotide, whereas the viruses isolated in Wuhan have a cytidine nucleotide in the corresponding genomic position (Fig. 1a). Moreover, from December 2019 to March 2020, a total of 210 complete viral genome sequences isolated in Wuhan and deposited in the GISAID database all had a cytidine nucleotide at nt 241 (data not shown). Interestingly, five coronaviruses isolated from pangolin (Manis javanica) in 2017 have a uridine nucleotide at nt 241, which is the same as SARS-CoV-2 in Beijing-Xinfadi (Fig. 1a). In contrast, the virus isolated from bat (Rhinolophus affinis) in 2013 (hCoV-19/bat/Yunnan/RaTG13/2013) has a cytidine nucleotide...
It appears that the mutation of this conserved pyrimidine nucleotide at nt 241 in the 5'-untranslated region of the viral genome occurred before the outbreak of COVID-19. This single pyrimidine nucleotide can serve as a biomarker to distinguish two major locally transmitted outbreaks of COVID-19 in China.

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**Conflict of interest**

None declared.

**Authors’ contributions**

LX conceived the study. YQP, ANB and FG collected and analysed the data. LX wrote the paper.
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