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| Curriculum

Pete and the Missing Scissors: a primary literature-focused case study that highlights the impact of SARS-CoV-2 on splicing

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ABSTRACT This case study was designed to help students explore the molecular mechanisms of the spliceosome and how SARS-CoV-2 impacts host cell spliceosomal function while interpreting figures from primary literature (A. K. Banjeree, et al., Cell 183:1325–1339, e1–e10, 2020, https://doi.org/10.1016/j.cell.2020.10.004). "Pete and the Missing Scissors" was designed and implemented in the spring of 2022 and fall of 2022 in two large-enrollment (150+) introductory molecular biology courses at a large, public research institution. The case study was formatted in alignment with the National Center for Case Study Teaching in Science (NCCSTS) framework, which has been shown to be an effective, student-centered approach to teaching complex biological concepts at the undergraduate level. The case study had four student learning objectives (SLOs) that aligned with Bloom's Revised Taxonomy and required students to develop an understanding of the molecular mechanisms of splicing and analyze and interpret a figure from primary literature. Both formative and summative assessment questions are included in this activity, with each question mapping to one of the case study SLOs. Summative assessment questions were given in a pre-/post-manner, and a paired *t*-test was used to evaluate differences between students' pre- and post-assessment scores. Assessment results demonstrated that students in both courses mastered each of the SLOs of this case study, given the significant increase in post-assessment scores compared to the pre-assessment. These findings indicate that the "Pete and the Missing Scissors" case study is an effective approach to develop students' understanding of the spliceosome, as well as ability to interpret figures from primary literature.

KEYWORDS case study, undergraduate biology education, SARS-CoV-2, spliceosome, mRNA, primary literature

The COVID-19 pandemic has had profound effects on higher education (1, 2), making it a relevant lens through which to study molecular biology. The pandemic is unique in the scale and speed with which data, and misinformation, were collected and distributed, shaping public health decisions and communication (3, 4). Simultaneously, the curiosity of life science majors about the molecular mechanisms of the virus grew, and as a result, SARS-CoV-2 has become an interesting educational model to teach biological topics.

The central dogma of molecular biology is a critical concept for undergraduate biology majors to master, serving as a core foundation for further biological study (5). Often covered in a traditional lecture environment, students may fail to master and retain these foundational concepts in the absence of active learning pedagogies (6–8). Additionally, the *Vision & Change* report (5) has highlighted the need to develop scientific competencies in life science majors in order to prepare them for modern careers, such as reading and interpreting scientific literature. For these reasons, we developed a narrative case study approach for students to learn about key elements of the central dogma of molecular biology, namely, mRNA splicing, that also helps students develop introductory

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skills associated with interpreting figures from primary scientific literature published by Banerjee et al. (9).

Case studies are an effective approach to promote student learning (10). Specifically, case studies often require students working in small groups to review data and/or evaluate real-world events, discuss approaches or interpretations of the case, and respond to questions that promote students' exploration of a specific topic (10–12). The use of case studies results in more significant gains in student learning compared to traditional approaches, particularly in introductory biology courses (13–15), and can be one of many approaches to infuse student-centered, active learning pedagogies into large-enrollment courses (16–18). In many instances, students are encouraged to connect cutting-edge research discoveries to concepts taught in the classroom, helping solidify new knowledge development, aid information retention, and improve learning gains (13). There are numerous published case studies available for instructors to use, including those available through the National Center for Case Study Teaching in Science (NCCSTS) (19). Since the start of the pandemic, there have been more than 10 case studies published to the NCCSTS related to SARS-CoV-2 or COVID-19 (NCCSTS database search performed on 11 July 2023).

For our case study, we chose to focus on the molecular mechanisms of the spliceosome, as Banerjee et al. published a paper describing how the SARS-CoV-2 protein NSP16 suppresses host mRNA splicing (9). mRNA splicing is a critical biological process necessary for the proper post-transcriptional modification and subsequent translation of eukaryotic genes. The spliceosome is a large RNA-protein complex that catalyzes the removal of introns from pre-mRNA in the nucleus (20). In this process, noncoding sequences, known as introns, are removed and coding sequences, known as exons, are spliced together to create mature mRNA used for translation of the protein product. Thus, understanding the principles of splicing and how this process can be disrupted (e.g., via mutations or by viruses) is critical to understanding the central dogma of molecular biology. While other educational activities have focused on the central dogma of molecular biology and more specifically the molecular mechanisms of the spliceosome through a primary literature and/or case study approach (21, 22), our case study is the first to explore how SARS-CoV-2 impacts the spliceosome of host cells using figures from primary literature published during the height of the pandemic (9).

Our case study involves a young scientist having a conversation with their molecular biology expert family member, who uses a fictional analogy of a pair of scissors cutting an individual's hair to represent the spliceosome modifying the pre-mRNA molecule. The impact of the SARS-CoV-2 NSP16 protein on the spliceosome (9) is represented in the analogy when the scissors necessary for an individual's haircut go missing, and thus, a haircut cannot be performed. We chose to use an analogy for our case study given the role that analogies play in helping students visualize complex and oftentimes invisible biological concepts (23–25). In the context of the analogy presented in our case study, students analyze a pivotal figure from Banerjee et al. (9) that depicts the NSP16 protein from SARS-CoV-2 disrupting the spliceosome of the host cell.

Intended audience

The intended audience of this activity is first- and second-year college biology and other life science majors enrolled in an introductory cellular and/or molecular biology course. This case study is appropriate for both small (e.g., less than 30) and large (e.g., greater than 120) course enrollments.

Learning time

This case study was designed to be implemented in a single, 50-minute class period. Prior to students completing the case study during class, they will complete a pre-class assignment that should take approximately 15 minutes.

Prerequisite student knowledge

Prior to this case study, students should have a foundational understanding of the central dogma of molecular biology to include the basics of transcription and translation in eukaryotic cells and where these processes take place. Advanced prior knowledge of the spliceosome is not required, although students should understand the difference between the template and coding (or non-template) strands of DNA and the role of these strands in gene expression. Additionally, students should understand the general gene structure and features of mature mRNA (including the Kozak consensus sequence), as well as the basics of protein structure. Finally, students should have had a previous introduction to experimental design to include the purpose of a positive and negative control and the difference between independent and dependent variables.

Learning objectives

Upon completion of this case study, students will be able to do the following:

1. Explain the molecular mechanisms of splicing.
2. Predict how alterations to the spliceosome affect the generation of mature mRNA transcripts.
3. Analyze and interpret a figure from primary literature.
4. Design a strand of pre-mRNA in a cell whose spliceosomal components have been disrupted.

Refer to Table 1 for Bloom's Taxonomy levels (26) associated with each of the student learning objectives (SLOs).

PROCEDURE

Materials

All materials for this case study are available in the supplemental materials. For this case study, students will need the case study pre-class assignment (Supplemental S1) and case study worksheet (Supplemental S2). Faculty will need the following: case study key (Supplemental S3), slides to use during class (Supplemental S4) that include a set of challenge questions for in-class formative assessment of student learning, and summative assessment questions (Supplemental S5) that can be included on a quiz or unit exam. No additional materials are required.

Student instructions

Students, working individually, should complete the pre-class assignment before the class period that this case study will be implemented in. The pre-class assignment (Supplemental S1) involves students watching short YouTube videos (27, 28) and is accompanied by a set of multiple-choice questions, which we recommend posting to

TABLE 1 Mapping of summative assessment questions to student learning objectives (SLOs) and Bloom's levels

Summative assessment question	Student learning objective (SLO)	Bloom's level
1	SLO-1: explain the molecular mechanisms of splicing.	Understand
2	SLO-2: predict how alterations to the spliceosome affect the generation of mature mRNA transcripts.	Evaluate
3	SLO-3: analyze and interpret a figure from primary literature.	Analyze
4	SLO-4: design a strand of pre-mRNA in a cell whose spliceosomal components have been disrupted.	Create

the course learning management system (LMS) as a quiz for students to complete. The student version of the case study (Supplemental S2) should be made available to students before class by posting on the course LMS, and students should be instructed to either download and/or print the case study before class.

During class, students should form teams of two to four to work on the case study. Faculty wishing to collect student responses to the case study questions are encouraged to have students complete the activity digitally so that students can upload their completed case study to the course LMS upon completion. The case study (Supplemental S2) is divided into five sections, with student teams working through each section before pausing to re-group as a class to complete one or more multiple-choice challenge questions individually via in-class polling software. The case study has clear instructions on where student teams should stop for these questions.

Faculty instructions

In advance of the lesson, the instructor must post the materials to the course LMS and devise a plan for collecting students' pre-class assignments. The pre-class assignment is designed to be a formative, low-stakes assessment to allow the instructor to evaluate students' prerequisite understanding of basic spliceosomal activity in eukaryotes. Again, we recommend that faculty set up a quiz of the multiple-choice pre-class activity questions in their course LMS for easy grading and review. The answer key for these multiple-choice pre-work questions is available in Supplemental S3.

Slides for faculty to use during the class session are available in Supplemental S4, and these slides provide suggested timelines for each of the five portions of the case study performed during class time. Again, this activity was designed to be implemented in a single 50-minute class session. The slides also include formative challenge questions (with answers) that the instructor can ask via polling software, with each of the five parts of the case study having one to two challenge questions for the students to complete. These formative challenge questions serve multiple purposes: (i) students gauge their own learning from the case study by completing related practice problems, (ii) formative questions allow for clarification of any misconceptions as the students work through the case study, and (iii) the questions promote engagement in the case study in large-enrollment courses, as student responses (collected through polling software) count toward participation points (graded on completion, not accuracy). The use of polling software specifically helps in high-enrollment courses as it cuts down on the grading burden associated with having students submit the case study at the end of the class for grading.

Representative answers to the case study (Supplemental S3) can be used by faculty to grade and/or evaluate student performance. Faculty wishing to collect student responses to the case study are encouraged to have student teams complete the case study digitally and upload their completed case study to the course LMS.

Suggestions for determining student learning

To evaluate students' mastery of the SLOs, formative and summative assessment questions have been developed. The challenge questions (Supplemental S4) in the case study slides serve as formative assessment questions that can be used during the class session in which the case study is implemented. Refer to Table 2 for the specific SLO

TABLE 2 Challenge question results (average ± standard deviation) from the fall 2022 implementation of this case study in the 100-level course (*n* = 156 students)

Case study part	Challenge question and SLO assessed	Average (± standard deviation) (%)
1	Q1: structure of mature mRNA (SLO-1)	55.1 ± 49.9%
2	Q2: protein structure (SLO-2)	92.3 ± 26.7%
3	Q3: positive vs negative controls (SLO-3)	83.3 ± 37.4%
	Q4: data interpretation (SLO-3)	86.5 ± 34.2%
4	Q5: maturation of mRNA (SLO-1)	87.8 ± 32.8%
5	Q6: NSP16 altered mRNA (SLO-4)	64.7 ± 47.9%

that each of the formative challenge questions assess. Supplemental S5 provides a set of summative assessment questions that can be used on a high-stakes assessment (e.g., quiz or unit exam) shortly after implementation of the case study. Each question assesses a specific SLO that is mapped to Bloom's Taxonomy levels (26) (Table 1).

Sample data

We implemented and assessed this case study in a 200-level molecular biology and genetics course in the spring of 2022 and in a 100-level cell and molecular biology course in the fall of 2022. All students in both sections watched the pre-class videos (27, 28) and completed the associated multiple-choice questions (Supplemental S1) via Gradescope (Turnitin, LLC), which they accessed through the course LMS. We found that most students in both courses received high scores (greater than 80%) on the pre-class assignment, with the answer key being available in Supplemental S3.

In the spring of 2022, representative answers to each of the questions were provided in the course slides that were used during the class period associated with this activity. Students were required to upload their submitted case study to the course LMS to earn participation points at the end of the recitation (graded for completion, not accuracy). In the fall of 2022, we added the challenge questions (Supplemental S4) to the course slides as a way to formatively assess student learning from the case study during class. These challenge questions were collected via Learning Catalytics (Pearson), with the results presented in Table 2. Representative answers to the case study questions can be found in Supplemental S3.

Safety issues

There are no safety issues associated with this case study, as this is not a lab-based activity.

DISCUSSION

Field testing

This project received exempt status from the University of North Carolina at Chapel Hill Institutional Review Board. This activity was implemented and formally assessed in two courses during a period of curriculum change within the UNC Department of Biology. The first course that this activity was implemented was in a 200-level molecular biology and genetics course that was part of the curriculum that will be phased out and no longer offered starting in the 2024–2025 academic year. The second course that this activity was implemented in was a 100-level cell and molecular biology course that is part of the new curriculum that was offered for first-year students starting in the 2022–2023 academic year. Depending on students' academic status, they took one or the other course (not both), and the prerequisite for both courses was a 100-level Principles of Biology course (or equivalent credit through advanced placement, or AP, examination).

For the 200-level course, this activity was implemented in a 50-minute recitation session in the spring of 2022. Each of the eight recitation sections had 24–30 enrolled students and was led by a graduate or undergraduate teaching assistant (TA). The lecture associated with this class met twice per week for 75 minutes and was co-taught by two PhD-level faculty members. The TAs met with the instructors weekly to discuss implementation of the recitations, including this activity. For this specific activity, the instructor reviewed the faculty instructions with the TAs, as presented above, and ensured that they had all of the required documents necessary to implement the activity. This course had four units total, with each unit culminating in a unit or cumulative final exam that assessed the learning objectives of that unit or course, respectively. Our activity was implemented in the second unit of the course (during week 6 of a 15-week semester) and was included in recitations that supported larger class discussions on the specifics of transcription in eukaryotes. Summative assessment questions were included on the unit 2 exam, which took place approximately 1.5 weeks after students completed this case study. A total of 232 life science majors, mostly at the sophomore level, were enrolled in the course that semester. Of these students, 163 students both consented to the use of their educational data for evaluation of this case study and completed both the pre- and post-assessments (Supplemental S5).

The second course included two sections of a 100-level cellular and molecular biology course that was taught by the same PhD-level faculty member in the fall of 2022. Both sections consisted of first-year, first-semester direct-entry, or transfer students, and the first section met for 50 minutes three times per week and had 141 enrolled students. The second section met for 75 minutes twice per week and had 136 enrolled students. This course also had four total units, with each unit culminating in a unit or cumulative final exam. The case study was implemented in a single class session of the 100-level course within the final two weeks of a 15-week semester (after the third unit exam), after numerous discussions about the central dogma of molecular biology. Summative assessment questions from this activity were included in the final exam, which took place approximately 2–3 weeks after the completion of this case study. Of students enrolled in both sections of this 100-level course, 181 students both consented to the use of their educational data and completed both the pre- and post-assessments.

All students in both the 200-level and 100-level courses completed the pre-class activities (Supplemental S1) individually prior to the class period in which the case study was implemented. The multiple-choice questions associated with the pre-class activities were posted to Gradescope, which students accessed through the course LMS (Sakai for the spring of 2022; Canvas for the fall of 2022). During the class session in which the case study was implemented, students worked in teams of two to four on the in-class portion of this case study activity. Students in the 200-level course submitted their completed case studies at the end of the class session, which were graded for completion, not for accuracy of the students' responses since the representative answers to the case study questions were made available during the in-class discussions throughout the session that the case study was implemented.

The challenge questions in the case study slides (Supplemental S4) were not included in the spring of 2022 but were added in the fall of 2022 as a modification to the case study. The purpose of adding these challenge questions was to provide an opportunity for formative feedback so that the instructor could evaluate student learning from the case study and clarify any misconceptions in a large-enrollment course environment in real time.

Evidence of student learning

The challenge questions implemented in the fall 2022 section of the 100-level cell and molecular course served as a formative assessment of the case study objectives. Each of the five parts of the case study had one to two challenge questions (Supplemental S4) that were asked via in-class polling software (Learning Catalytics). As shown in Table 2, students scored greater than 50% correct on each of the challenge questions. Students performed the best (80% correct or more) on the formative challenge questions associated with SLO-2 and SLO-3. This was not surprising given that both objectives have been covered in detail previously in the course before this case study was implemented. Students in the 100-level course struggled the most on formative questions associated with SLO-1 and SLO-4 (Table 1). While it was not surprising that students struggled with the formative question associated with SLO-4 given that this was the first time that this objective had been covered in the class, it was somewhat surprising that students struggled with the formative question associated with SLO-1 because this concept was previously covered and assessed on the unit exam immediately before this case study was implemented. We suspect that because challenge question 1 presented information related to SLO-1 in a different context, specifically in the context of a case study, students struggled to make connections to previous learning in order to answer this question (29, 30). Thus, students may need some additional guidance and reinforcements to make connections to previous content, especially when presented in a different context. The challenge questions presented in Supplemental S4 were not included in the case study that was implemented in the 200-level course in the spring of 2022.

In addition to the abovementioned formative assessments, the SLOs of this case study were summatively assessed in both the 100-level and 200-level courses. Before students engaged in the case study in both semesters, students responded to the summative assessment questions (Supplemental S5) that mapped to the case study SLOs (Table 1), which served as the pre-assessment for this activity. Students were required to respond to these questions, although they were not graded, nor did they receive the results from this pre-assessment. Students in the 200-level course took the pre-assessment the first week of the semester during their initial recitation, approximately 5 weeks before the case study was implemented. Students in the 100-level course took the pre-assessment during class 1 week before the case study activity took place. The pre-assessment was completed online in an in-person proctored environment during class time. Students then received the same questions after completion of the case study on a unit (200-level course) or final (100-level course) exam and were graded for accuracy in their response. We analyzed differences in scores using a paired *t*-test ($P < 0.05$) to evaluate student attainment of the case study SLOs. Results of this analysis demonstrated that the learning outcomes of the case study were achieved (Fig. 1 and 2).

In the 200-level molecular biology and genetics course, assessment results revealed that students demonstrated competency in explaining the molecular mechanisms of splicing and predicting how disruptions to this process may affect mature mRNA transcripts (SLO-1 and SLO-2, respectively). This was demonstrated by significant gains on the post-assessment for questions 1 and 2 compared to the pre-assessment (Fig. 1). Similar observations were also made for SLO-3 and SLO-4 (which were assessed by questions 3 and 4, respectively), in that the post-assessment scores were significantly higher than the pre-assessment scores (Fig. 1). Interestingly, we observed the strongest gains in this 200-level course associated with question 2, which assessed SLO-2 (Fig. 1). Again, while we observed significant gains for all other questions, we noticed that the pre-assessment scores for questions 1 and 3 (assessing SLO-1 and SLO-3) were high (greater than 50% correct), suggesting that students in the 200-level course had prerequisite knowledge related to these SLOs. Given that the case study in this 200-level course was implemented in TA-led recitation sections consisting of 24–30 students, these results demonstrate the effectiveness of this case study in promoting student learning in smaller learning environments.

In the 100-level cell and molecular biology course, students displayed competency in all SLOs, demonstrated by significant gains for all four assessment questions when

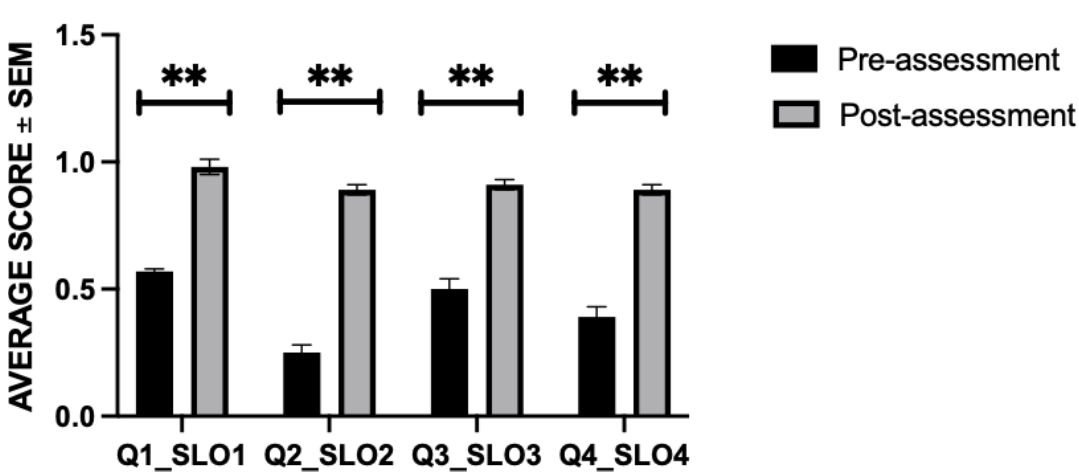

FIG 1 Assessment results from the 200-level molecular biology and genetics course. Pre- and post-assessment scores ($n = 163$ students) for each of the four questions that assess the case study SLOs. Each question was worth one point, with the average and standard error of the mean (SEM) depicted. Data were analyzed using a paired *t*-test (GraphPad Prism software), where ** denotes $P < 0.0001$.

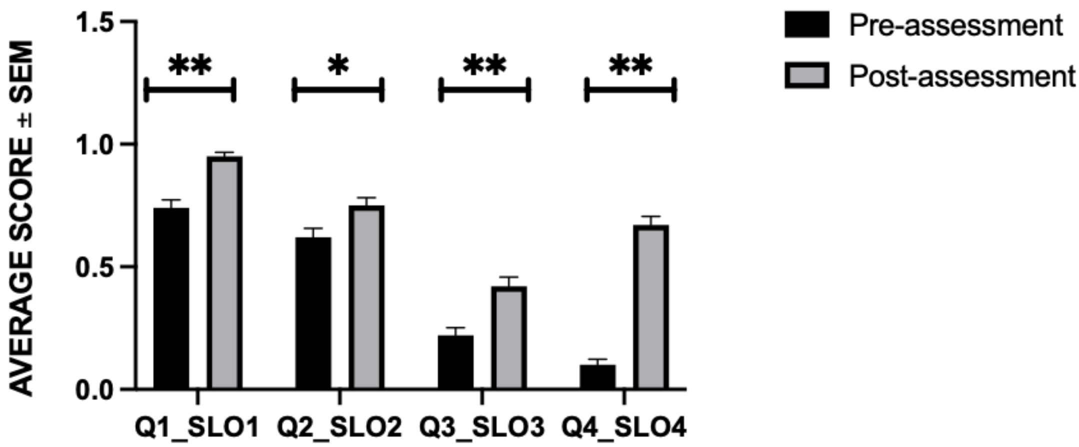

FIG 2 Assessment results from the 100-level cellular and molecular biology course. Pre- and post-assessment scores (n = 181 students) for each of the four questions that assess the case study SLOs. Each question was worth one point, with the average and standard error of the mean (SEM) depicted. Data were analyzed using a paired t-test (GraphPad Prism software), where * denotes $P < 0.01$ and ** denotes $P < 0.0001$.

comparing the pre-assessment to the post-assessment (Fig. 2). In the 100-level course, we observed high pre-assessment scores (greater than 50% correct) associated with questions 1 and 2 (assessing SLO-1 and SLO-2, respectively), suggesting that students in this cohort had prerequisite knowledge relating to these SLOs. This was anticipated given that this case study was implemented at the end of the semester after numerous conversations related to the central dogma of molecular biology. Modest gains were observed for question 3, assessing SLO-3. This was somewhat surprising given that the objective of analyzing and interpreting data from primary literature had been covered extensively throughout the course. The greatest gains for the 100-level cohort were associated with Q4, which assessed SLO-4 (Fig. 2), an SLO that had not been previously covered in the course. Since the case study was implemented by PhD-level faculty in a lecture section of approximately 140 students, these results show that this case study is also effective in a large course-enrollment classroom.

Overall, student gains were lower in the 200-level course compared to the 100-level course, which can be explained by multiple factors. First, we made changes to the assessment questions between the spring of 2022, when the 200-level course completed the case study, and the fall of 2022, when the 100-level course completed the case study. These changes were made to better align with the assessment levels of Bloom's Taxonomy. Refer to the summative assessment questions (Supplemental S5) for the questions used to address the case study SLOs in the fall of 2022 (spring of 2022 assessment questions available upon request). Additionally, the 200-level course consisted of second-year students or higher, who likely had greater practice with interpreting data from primary literature sources from previous coursework compared to those in the 100-level course, which consisted of first-year, first-semester direct-entry, or transfer students.

Possible modifications

Refer to Supplemental S6 for possible modifications for this case study activity.

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ADDITIONAL FILES

The following material is available online.

Supplemental Material

Supplemental materials S1 to S6 (jmbe00123-23-s0001.pdf). All supplemental materials combined into a single document.

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