An active approach to primary literature & the scientific process in undergraduate classes

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Why understanding the primary literature is a challenge for undergraduate students

- Vocabulary used – challenging "regular" language & scientific jargon
- Introduction rarely written at an undergrad level
- Students not familiar with the science &/or the techniques
- Students read the authors' interpretations, before/instead of interpreting the data for themselves

Reading a journal article, on their own, is a difficult assignment for undergrads!

Eliminate some of these barriers using a flipped approach to the scientific literature

→Assign pre-class readings that students can understand

→ Use in class time to focus on the science in the paper, using active learning

General strategy to active learning approach to scientific literature

1. Assign a pre-class reading(s) of an appropriate level
2. Fill in gaps related to background information during class meeting
3. In class, students brainstorm about questions to be addressed & experiments to be done
4. Reveal data from the paper for students to interpret
5. Synthesis activity/assessment

All of this is done without reading the text of the journal article!

An example of how I've used this strategy

- Molecular biology of human health conditions course – mostly juniors & seniors
- 1.5 hour session

ARTICLE

doi:10.1038/nature12394

Translating dosage compensation to trisomy 21

Jun Jiang[1], Yuanchun Jing[1], Gregory J. Cost[2], Jen-Chieh Chiang[1], Heather J. Kolpa[1], Allison M. Cotton[3], Dawn M. Carone[1], Benjamin R. Carone[1], David A. Shivak[2], Dmitry Y. Guschin[2], Jocelynn R. Pearl[2], Edward J. Rebar[2], Meg Byron[1], Philip D. Gregory[2], Carolyn J. Brown[3], Fyodor D. Urnov[2], Lisa L. Hall[1] & Jeanne B. Lawrence[1]

- Prior knowledge of students: molecular basis of Down syndrome & the over-expression of genes on chromosome 21, but they have not learned details about X chromosome inactivation

1. Assign a pre-class reading(s) of an appropriate level

X Chromosome: X Inactivation

By: Janice Y. Ahn (*Harvard Medical School*) & J. T. Lee, Ph.D. (*Department of Genetics, Harvard Medical School*) © 2008 Nature Education

Citation: Ahn, J. & Lee, J. (2008) X chromosome: X inactivation. *Nature Education* 1(1):24

Females (XX) carry twice as many X-linked genes on their sex chromosomes as males (XY). How do cells control gene expression to manage this potentially lethal dosage problem?

Aa Aa Aa

Unlike the gene-poor Y chromosome, the X chromosome contains over 1,000 genes that are essential for proper development and cell viability. However, females carry two copies of the X chromosome, resulting in a potentially toxic double dose of X-linked genes. To correct this imbalance, mammalian females have evolved a unique mechanism of dosage compensation distinct from that used by organisms such as flies and worms. In particular, by way of the process called X-chromosome inactivation (XCI), female mammals transcriptionally silence one of their two Xs in a complex and highly coordinated manner (Lyon, 1961). The inactivated X chromosome then condenses into a compact structure called a Barr body, and it is stably maintained in a silent state (Boumil & Lee, 2001).

A prime example of X inactivation is in the coat-color patterning of tortoiseshell or calico cats (Figure 1). In cats, the fur pigmentation gene is X-linked, and depending on which copy of the X chromosome each cell chooses to leave active, either an orange or black coat color results. X inactivation only occurs in cells with multiple X chromosomes, which explains why almost all calico cats are female.

X inactivation exists in two different forms: random and imprinted. Although both forms utilize the same RNAs and silencing enzymes, they differ in terms of their developmental timing and mechanism of action.

Figure 1: Calico cat.
The patchy distribution of color on calico cats results from the random inactivation of one X chromosome in females. Ksmith4f via Wikimedia Commons.

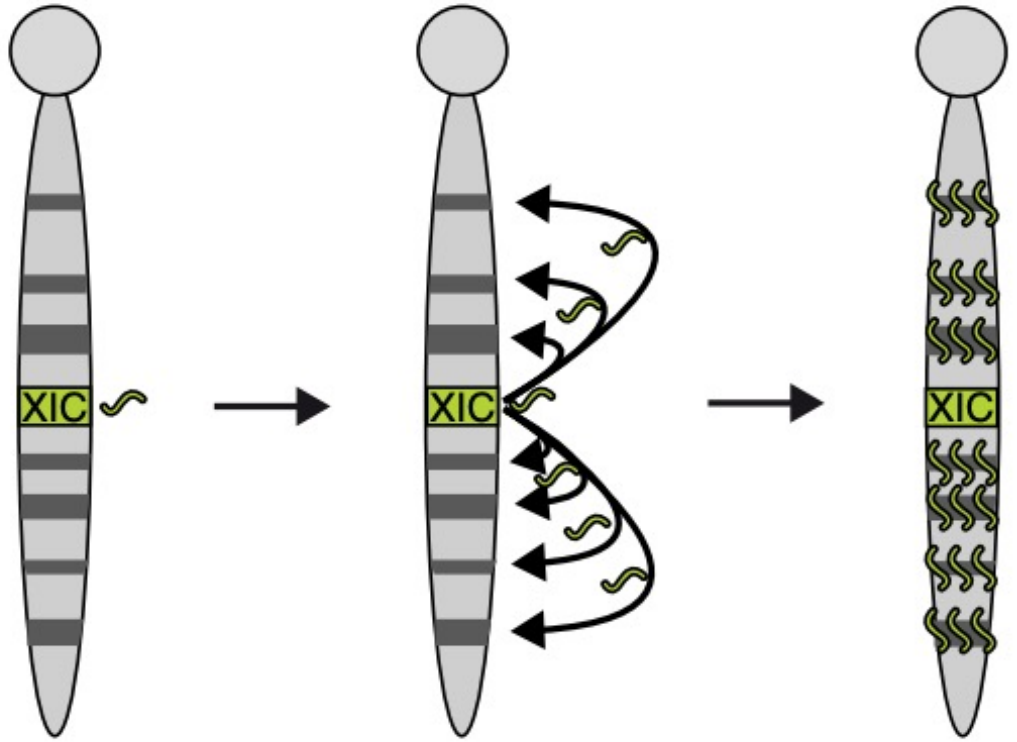
Nature Scitable

*Study questions to accompany reading

2. Fill in gaps related to background in class

- Go over answers to study questions

- Discuss molecular details of X chromosome inactivation, including changes in chromatin structure – based on a review article that they do not read



Cerase et al. 2015

3. In class, students brainstorm about questions to be addressed & experiments to be done

- Students work in groups of 3-4, followed by class discussion
- At this point, I do not ask them to design experiments

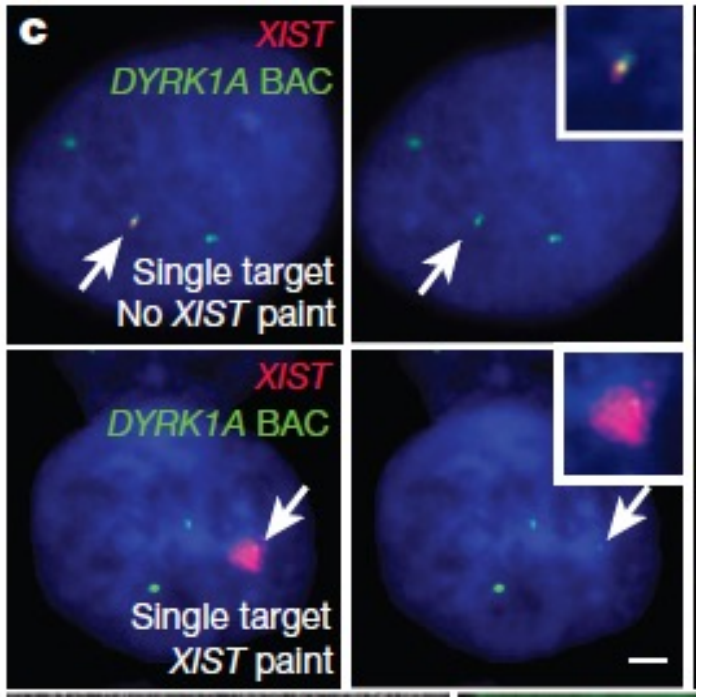
- How might the *XIST* gene be used as a genetic therapy for Down syndrome?
- In general, what might you expect if the *XIST* gene were inserted in an autosome?
- What kinds of molecular features might you expect for that autosome carrying the *XIST* gene?

→ I compile a list of collective student answers to the third question on the board

4. Reveal data from the paper for students to interpret

- One data set at a time
- Annotate figures & add critical information (no figure legends or text)
- Small group discussion, followed by class discussion

DNA/RNA FISH



DYRK1A is a gene on chr 21.

Targeted questions to guide students:

→How many copies of chr 21 are found in these cells?

→How many copies of chr 21 carry the transgenic *XIST?*

Jiang et al. 2013

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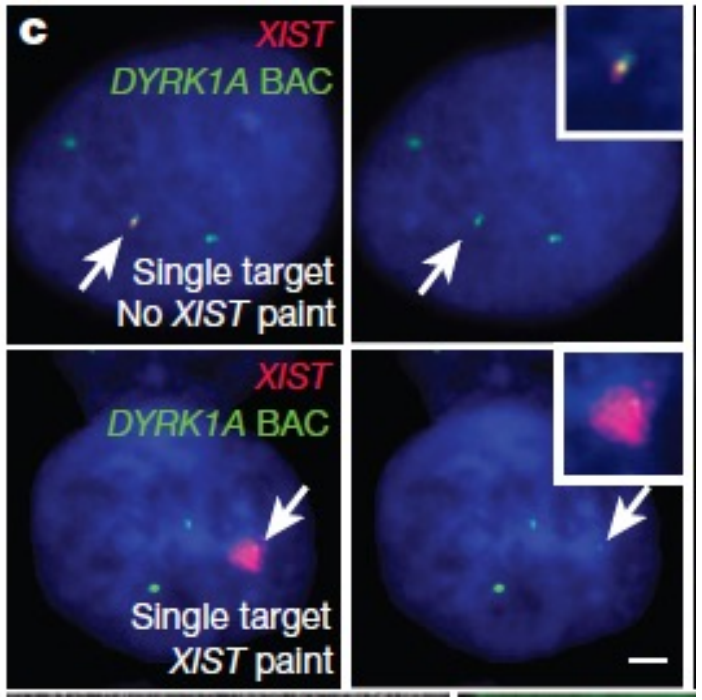

DYRK1A is a gene on chr 21.

Check off student answers from list as data from paper are discussed!

Jiang et al. 2013

5. Synthesis activity/assessment

- Write abstract based on data discussed in class – this is my favorite!
- Plan a follow up study
- Describe the most interesting part of the paper
- Write at least one question about X chromosome inactivation &/or the experiments discussed today

Advantages to this active approach

- Students are immersed in higher-level critical thinking during class:
  - Developing scientific questions & forming hypotheses
  - Designing experiments, including controls
  - Data analyses & drawing conclusions
- More opportunities for SUCCESS with experimental design
- Opportunities to discuss how real science is done & to consider feasibility – students often suggest experiments that are not done
- Allows gaps in knowledge to be identified more readily
- Student investment in the paper!

Adapt to any level & all scientific disciplines

- Tailor questions to appropriate level during brainstorming & interpretation phases
  - Ask students for control(s)
  - Ask students to make predictions before data is revealed
- Students can think of questions to address, even if they don’t know the techniques to do it
- More or less writing as an assessment at the end

Questions?

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