Addgene: a global resource working to enhance scientific reproducibility

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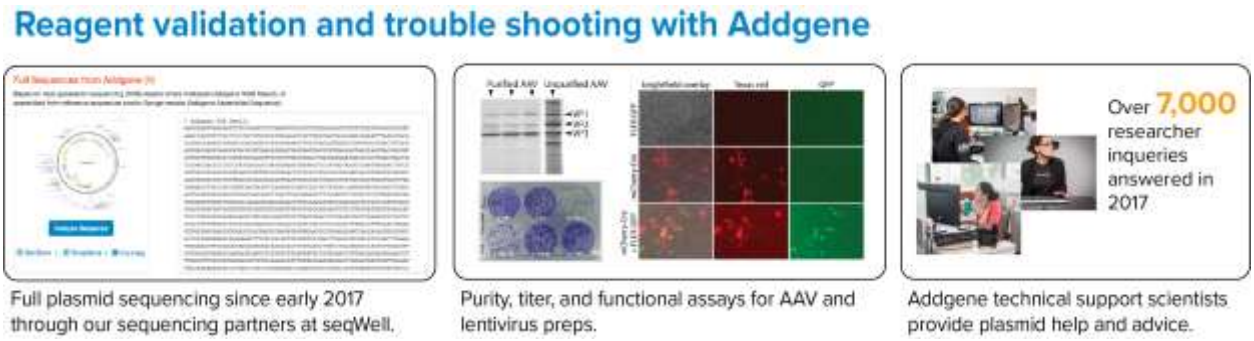
Reproducibility, here defined as the ability to apply published research findings to future work, is key to the successful and efficient advancement of science. There are many tools available to help researchers make their work reproducible. These tools enable users to think carefully about experimental designs, to explicitly and tenaciously describe experimental procedures, and to easily/effectively share the results of their work. Addgene provides many such tools to help make research more reproducible. Indeed, Addgene's primary role in reproducibility is to make it easier for researchers to share reagents, but Addgene also interacts with many other aspects of reproducibility in important and subtle ways. Addgene validates reagents, provides access to resources that make it easier to use reagents, and enables researchers to quickly find the proper tools for their work so they can spend more time thinking about experimental design.

Reagent Validation - Promoting Reproducibility through Addgene's Core Mission

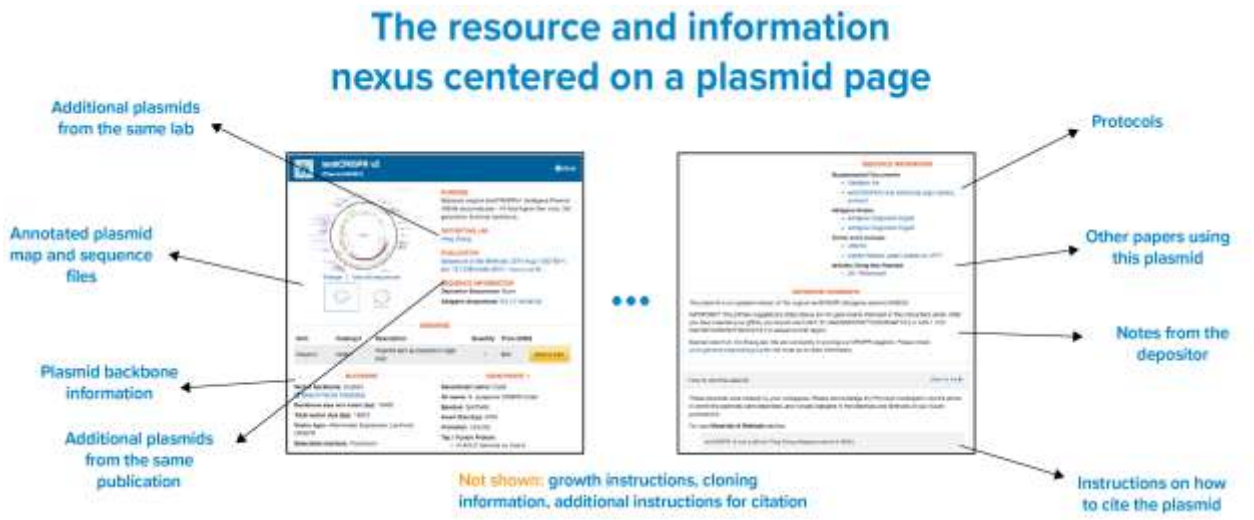
Addgene's mission is to accelerate research and discovery by improving access to useful research materials and information. Reproducibility is intimately intertwined with this mission; to accelerate science, tools available from Addgene must function as described.

To help ensure that the materials we distribute on behalf of researchers across the globe are reliable, we validate them in various ways. For plasmids, we perform DNA sequencing (full plasmid sequencing since early 2017). For viral preps, we sequence the DNA in the viral particles, titer the viruses, and occasionally perform functional tests. With these validation steps and the addition of more comprehensive plasmid maps to our website, researchers who request plasmids from Addgene can be quite confident in the integrity of what they've requested.



At its core, Addgene also overcomes the relatively simple but burdensome barriers of good tracking and record keeping that make it difficult for individual labs to share their reagents in reproducible ways. This is in stark contrast to the status quo before Addgene wherein a fellow scientist who was already strapped for time and funding would be forced to dig through past researchers' rarely annotated or validated freezer stocks. Of course this meant that many scientists would be sent the wrong reagents resulting in wasted time, money, and duplicated work - the essence of irreproducibility. Addgene's mission promotes reproducibility at this basic but incredibly important level.

Improving access to protocols and other additional sources of reagent information



Having the proper reagent in hand does not necessarily mean that you will be able to use it correctly without extensive troubleshooting. Addgene therefore provides resources that make it more likely that you'll be able use reagents deposited with us successfully and efficiently.

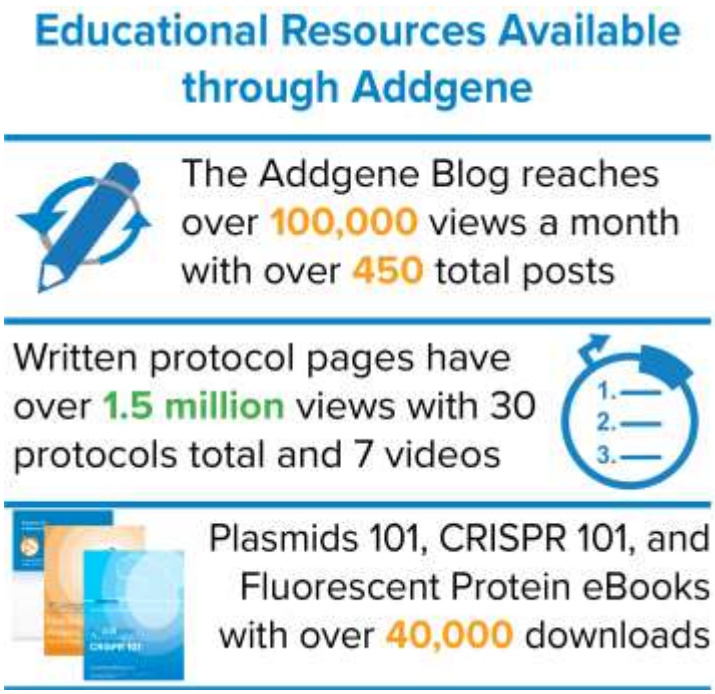
Many plasmids are transferred between researchers with few instructions but plenty of practical wisdom about how to use them. You've probably used a plasmid or other reagent at some point having no idea how it was created or what it was originally used for. Knowledge of something as simple as how a plasmid got its name can be quickly lost as reagents are passed between generations of

graduate students and postdocs (naming plasmids in a systematic way can at least help you retain some information). This imperfect knowledge transfer can make it very difficult to troubleshoot an experiment using a particular reagent. You might, for example, find it hard to figure out why your gene of interest is failing to express or why your cells start dying.

Addgene provides multiple ways for researchers to learn about the reagents available from the repository. First, roughly 80% of plasmids available through Addgene have papers associated with them and links to these papers can be found directly on the plasmid's page on addgene.org. The paper originally describing the creation of a material is the best place to start to understand how to use it properly. In addition, Addgene encourages depositors to upload further information including descriptive protocols and sometimes even sample data. Like the associated publication, these resources can be found directly on a plasmid's page on addgene.org. Finally, researchers can find publications that have used a given material through the "Articles citing this plasmid" section of a material's page. These publications can provide researchers with examples of the various ways a plasmid can be used and may alert them to any troubleshooting issues thereby avoiding repeated work.

Ultimately, Addgene plasmid pages form the focal point of a nexus of resources that researchers can use to help them successfully use materials available from the repository. We're always looking for ways to improve these pages and improve their connections to other resources.

Educational Resources to Help Researchers Find the Right Tools for the Best Experimental Designs



Many practices that promote reproducibility - pre-registration of experiments (Nosek et al 2018), good statistical practices (Sterling 1959, Ioannidis 2005, Button et al 2013), and proper recording of methods (Teytelman et al 2016) to name a few - rely on thoughtful experimental design for effective implementation. It can, however, be difficult to focus on these things when you need to make or test out many model systems and tools before you even get a set of experiments off the ground. Educational resources, which are freely available at addgene.org, both provide researchers with tips on how to perform their experiments effectively and direct researchers to the best tools for

their specific needs, thereby freeing up resources and time for experimental design.

Written protocols available at addgene.org provide step-by-step instructions on how to do a variety of simple laboratory techniques with tips on possible pitfalls and ways to use these techniques more efficiently. These protocols walk through procedures that researchers often learn through spoken instruction and for which there often isn't enough detail to avoid simple mistakes that can ruin entire experiments. Our "Pouring LB Agar Plates" protocol, for example, provides tips on how to avoid degrading your antibiotic and how to keep track of your plates while also walking through the importance of testing plates once they're solidified. These simple steps could keep you from wasting an entire week of cloning simply because you plated something on a faulty LB/agar plate.

We've also begun making video counter-parts to our written protocols. These videos provide viewers with an additional level of detail and can give a researcher more confidence in the proper way to perform a technique. To date our protocol videos have over 80,000 views and we'll be creating many more videos including additional short "Lab Tip" videos as time goes on.

Once you have "basic" protocols down, you can start designing experiments directed towards testing a specific hypothesis or answering a particular research question. However, even with a phenomenally interesting research question, it's not always easy to find what tools are available to help you answer this question. Research papers aren't often structured in ways that make it easy to search for particular reagents (especially when there are large supplemental methods sections) and it might not be clear from something like an abstract or paper title that a useful reagent is even contained in a paper.

Addgene makes it easier for researchers to find the reagents they need for their experiments by curating plasmids and viruses according to their uses. Whether you're purifying a protein from *E. coli* or expressing a receptor in mammalian cells, you can quickly find the plasmids that make the most sense for your work by browsing our curated collections pages or using the search functionality on addgene.org. If neither of these leads you to the type of reagent you're looking for, you can even email or call us and one of our scientists will provide additional help.

Other educational resources available from Addgene highlight the potential usefulness of specific reagents available from the repository and connect researchers to the background information necessary to work with recently developed technologies. For example, hot plasmid articles break down how new plasmid technologies were developed, what they've been used for, and how you can use them in the future. Our free eBooks and guide pages further dive into the details of exciting technologies like CRISPR or fluorescent proteins thereby connecting you with trouble shooting tips and ideas for experiments that might help you answer your specific research question.

These various educational resources enable researchers to spend more time on experimental design by explaining the basics behind new technologies and quickly connecting them to the appropriate literature where they can learn more if necessary. Plasmids highlighted in our educational

resources are usually directly available from addgene.org enabling a researcher to order them quickly and avoid lengthy plasmid design and construction steps while gaining access to suggestions for procedures and assays that can be used with that particular plasmid.

Troubleshooting and validation will always be necessary for a new experiment. Despite that,we hope that our extensive linking to other resources combined with frequent updates will greatly decrease the time researchers spend searching the literature, troubleshooting, and wondering if an exciting new technology is applicable to their preferred system.

Collaborations to further enable reproducibility

Addgene scientists are working on many initiatives that we hope will further promote and enable reproducibility. We are collaborating with organizations like Protocols.io, eLife, and Code Ocean to create workshops that introduce researchers to reproducibility issues, solutions, and their associated tools. We encourage journals to promote the deposition of research materials in repositories. Addgene is a registered RRID organization and our repository is currently recommended by 30 journals. We also actively promote conversations about broad changes to the research enterprise that will incentivize reproducibility. These changes include but are not limited to checklists (Han et al 2017), preprints, and pre-registration of experiments (Nosek et al 2018).

Beyond these concrete initiatives, we use our social media presence to participate in and promote conversations around reproducibility generally and to quickly solve potential problems with materials available from the repository in particular. A great example of this is our involvement in the conversation surrounding the now defunct genome editing tool NgAgo. This tool was deposited to Addgene and, based on the publication originally describing it, scientists predicted it might be better than CRISPR. Many researchers soon tested NgAgo and refuted its usefulness all the while citing Addgene as their source of NgAgo plasmids (Burgess et al, Lee et al, Javidi-Parsijani et al). It is likely due to its availability through Addgene that these researchers were able to test NgAgo so quickly and we worked directly with members of the Addgene community (Pooran Dewari in particular) to learn more about issues with this seemingly promising technology. After realizing that the hype surrounding NgAgo was too good to be true, we publicized this information widely through our blog and social media platforms.

Looking forward to a reproducible future

Addgene and other organizations are working hard to equip researchers with the tools they need to make their work more reproducible. We hope that researchers can use these tools to save time, spend more resources on thoughtful experimental design, and thereby generate findings that will advance knowledge. Not only will this make the research process more efficient, but it will give scientists and non-scientists alike more faith in the scientific enterprise.