Addgene – A Unique Nonprofit Helping Accelerate Science

Joanne Kamens, PhD
Addgene, Executive Director
Addgene Helps Scientists Share Plasmids

We promote collaboration and sharing by making it easy to share plasmids
(and some other types of research materials)
What is a Plasmid?

- Scientists study and manipulate genes using plasmids.
- Chromosomes are long and complicated—when scientists want to study just one gene, they cut the gene out of the chromosome and put it in a plasmid.
- A plasmid is a circle of DNA 3-4 orders of magnitude smaller than a chromosome.
Easier Collaboration Means Better Science

Requestor Benefits

- Excellent customer support
- Timely receipt of materials from many labs in one order
- Quality control / data curation improves reproducibility
- International access to 85 countries so far!
- Plasmid selection and design assistance
- Educational Resources
"I do science differently now that I can request plasmids from Addgene"  
Lab head at Yale

Over 11,000 plasmids distributed each month!

“Scaling” of a centralized resource enables additional/improved services.
Addgene’s Nonprofit Mission

Accelerate research and discovery by improving access to useful research materials and information

Why be a nonprofit?

- Ensures the trust of scientists, tech transfer offices and attracts other partners
- Allows Addgene to make decisions based on what is good for scientists (which includes making sure we are financially sound)
- Results in excellent employee culture and morale
Addgene aims to be the best and most widely used open-access platform for educating scientists about plasmid-based technologies.

Transforming Scientific Training

Build educational resources by curating existing data, optimizing published protocols, and working with our large network of experts.

Share information via Addgene’s website, blog, videos, podcasts, and open-access articles.
# Educational Impact – Early Results (2015)

Addgene’s Impact on Various Educational Resources for the Scientific Community

<table>
<thead>
<tr>
<th>Educational Impact</th>
<th>CRISPR-Cas</th>
<th>Viral Vectors</th>
<th>Plasmids 101 &amp; Protocols</th>
<th>Science Careers</th>
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1 Released 1/16  
2 Released 10/14

Copyright
Addgene as a Global Resource

• 3 person Addgene London office established in 2014 to better serve European scientists
  • Office support provides extended customer service hours
  • Outreach Scientists visit universities all over Europe

Addgene partners with distributors in China, Japan and Korea
Depositing is Free and Easy
Growth of the Addgene Collection

Addgene is fantastic. I will forward your details to PIs in the Institute, that way potential plasmid donors will know you are around.
Depositor, University College Dublin

Addgene fast fact:
Plasmids have been deposited from all of the top 50 NSF funded research institutions

Oh so, you’re not really a salesperson, you’re here to make my life easier...
Future depositor, CHOP
Joining the Sharing Community

Depositing is Easy

• Addgene PhD scientists help during the entire process
• Deposit before publication so when the paper comes out, plasmid numbers are in the materials and methods
• Addgene takes care of entire tech transfer process

Depositor Benefits

• Saves time on request fulfillment, supported int'l sharing
• Archiving key reagents, protection against lab turnover
• Plasmids get used again, instead of frozen/lost
• **Increased exposure for the scientists**
Depositing in a Biological Resource Center Increases Citation Rates

“Climbing Atop the Shoulders of Giants: The Impact of Institutions on Cumulative Research.”
The electronic Materials Transfer Agreement

- Addgene pioneered a novel, online system to enable easier, faster transfer of biomaterials with legal documentation in place
- Each plasmid exchange results in a completed eMTA
- Addgene has facilitated >200,000 eMTAs since 2004

**Deposit Process**

1. Depositor completes deposit form
2. MTA emailed to Tech Transfer Office or Depositing PI
3. Authorized signature
4. MTA is approved
5. Stored materials are available to the scientific community

**Auto-approval if no special terms**

**Request Process**

1. Scientist places order online
2. Addgene emails MTA to TTO or PI
3. MTA is approved
4. Addgene ships material to scientist
And Then Came CRISPR

126 scientists have deposited CRISPR plasmids with Addgene.
The power and broad applicability of CRISPR technology is evident as CRISPR distribution outpaces other engineering technologies.
Where are CRISPR Related Materials Going?

Addgene has distributed >60,000 CRISPR plasmids to scientists in >80 countries:

- United States: 48%
- Japan: 14%
- China: 7%
- Germany: 5%
- Great Britain: 5%
- Canada: 3%
- Korea: 2%
- Switzerland: 2%
- France: 2%
- Australia: 1%
- Rest of World: 14%

Distribution of Addgene's Top 20 CRISPR/cas9 Plasmids

Also reflects percentage overall distribution for each country:
- Denmark ~ 0.5%
The Addgene CRISPR/cas9 Plasmid Collection

Scientists are figuring out new and clever ways to use this system to advance basic research.

Addgene helps to accelerate this rapid technology development.
Addgene hosts >100 educational online resource pages pertaining to CRISPR genome engineering.

These resources have been viewed over 1.8 million times.
CRISPR Plasmids Put to Work

>20 published papers already cite this one plasmid requested from Addgene (it was made available May, 2014)
Answering Unsolved Questions with CRISPR Screens

A CRISPR-Based Screen Identifies Genes Essential for West-Nile-Virus-Induced Cell Death

Hongming Ma*, Ying Dang*, Yonggan Wu, George Jiangua, Junli Zhang, Sojan Abraham, Jang-Gi Choi, Guoyan Shi, Ling Qi, N. Manjunath, Haoquan Wu*

*Co-first authors
“The Human Genome Project has yielded a fairly complete catalog of cellular components, and a major goal moving forward will be to classify all genetic elements involved in normal biological processes and disease. With advances in gene editing enabled by the CRISPR-Cas system, it is no longer quixotic to seek a comprehensive picture of cellular circuitry for human cells.”
Gene-edited pigs are protected from porcine reproductive and respiratory syndrome virus.
Tools for Genomic Tagging “in situ”

Mendenhall and Meyers Tagging System

The Eric Mendenhall and Richard Myers labs have deposited plasmids for a CRISPR-based system to add a tag (currently using FLAG) to endogenous proteins. This CRISPR/Cas plasmid system consists of two components:

- A vector containing Cas9 and a validated gRNA, based on the Zhang lab's PX458.
- Multiple gRNA plasmids may be used.
- The HDR (homology directed repair) donor plasmid with homology arms and selection marker.

The first deposited plasmids in this CRISPR-Cas tagging system were tested by tagging transcription factors with FLAG in human cell lines. To repeat the tagging in your system, use the plasmids as listed in each row. If your own gene of interest is currently unavailable, you will need to design and clone in a gRNA(s) to guide the Cas9 protein to your target sequence, as well as design and clone in the homology arms for the donor plasmid.

The Mendenhall and Myers labs have also provided their protocol for homology arm cloning:

Mendenhall & Myers FETCh-seq Protocol (134.7 KB)

Novel technology allows a gene to be tagged and tracked while it is still in its own location on the chromosome.
RNA-targeting Cas9
Another scientific breakthrough by Dr. Jennifer Doudna in collaboration with Dr. Gene Yeo
Addgene requested plasmids used for the studies.

- “An sgRNA sequence targeting the C terminus of G3BP1 was cloned into pSpCas9(BB)-2A-GFP (pX458) (gift from Feng Zhang; Addgene plasmid no. 48138)”
- “The dCas9-2xNLS sequence was amplified from pHRSFFV-dCas9-BFP-KRAB (a gift from Stanley Qi and Jonathan Weissman; Addgene plasmid no. 46911)”
Addgene’s Role in the Rapid Spread of CRISPR Technology

“The number of scientific papers with CRISPR in their title rose from 90 in 2012 to 741 (and counting) this year. That was partly Zhang’s doing: he has been using a non-profit called Addgene to distribute genetic and other material, called reagents, to biologists around the world.”

-STAT News

“The rapid adoption of the Cas9 technology was also greatly accelerated through a combination of open-source distributors such as Addgene.”

-Patrick Hsu, Eric Lander, Feng Zhang Cell 2014
How Can We Help?

✓ Twitter: @addgene
✓ Facebook: Addgene
✓ LinkedIn: Addgene
✓ blog.addgene.org
✓ help@addgene.org
✓ 617-225-9000
Example: CRISPR Library Screens

Recent blog by Horizon Biosystems “Seven Essential CRISPR Screening Papers”
All 7 use Addgene deposited or requested plasmids and libraries
“It’s hard to keep up with the rapidly expanding world of CRISPR, and it’s starting to feel like CRISPR screens are being published every week, taking the technique from the cutting edge to the mainstream.”
Better Tools for Screening, Faster Discoveries

CRISPR knockout screening outperforms shRNA and CRISPRi in identifying essential genes

Bastiaan Evers, Katarzyna Jastrzebski, Jeroen P M Heijmans, Wipawadee Grernrum, Roderick L Beijersbergen & Rene Bernards

- CRISPR screening outperforms the previous lead technology, shRNA
- Less variation, more constructs that worked, fewer off target effects
- Result: lower false positive rate, better consistency in different cell types