

## 2021 Drosophila White Paper

The first Drosophila White Paper was written in 1999. Revisions to this document were made in 2001, 2003, 2005, 2007, 2009, 2012 and 2016; these versions are available through the Drosophila Board [website](#). Here, the Drosophila Board of Directors presents an updated White Paper identifying and prioritizing current and future needs of the Drosophila research community, based on the input from community leaders and comments received from community members. This document is a resource and reference for the Drosophila research community, for national funding agencies (NIH, NSF), and for leaders in other fields of research, scientific communication, and education. This White Paper was approved by the Drosophila Board on **April 6th, 2022**.

### **Part I: Drosophila as an experimental system for research – past, present, and future**

Drosophila is a leading animal model for biomedical research and for understanding the basic biology of animal systems. Data and discoveries acquired from studies in Drosophila directly impact our understanding of evolutionarily distant metazoans, including humans and other vertebrates, as well as invertebrates such as insects that are of medical or agricultural importance.

Our understanding of the basic principles of genetics, including the nature of the gene, genetic linkage, meiotic chromosome segregation, recombination, and the appreciation that genetic information can be permanently altered by external insults such as X-rays all arose from studies in *Drosophila*, particularly *D. melanogaster*. Pioneering cloning studies with *D. melanogaster* that linked molecular lesions in the genome with mutant phenotypes led to the identification of many genes and their products that play essential and conserved roles in development and physiology of all animals including humans. Drosophila research has led to deeper understanding of fundamental biological processes, including the innate immune response, stem cell determination and maintenance, cell and tissue polarity, cell proliferation and growth control, pattern formation, organ morphogenesis and physiology, circadian rhythms, sensory biology, animal behavior, learning and memory, sex determination, fertility, neuronal pathfinding, meiosis and mitosis, interphase chromosome structure through the study of polytene chromosomes, synaptic transmission and evolution. Additional areas where Drosophila research has provided critical, fundamental insights include investigations of organ development and physiology, neural function that scales across genes and molecules to neural networks to behaviors, transcriptional regulation including cis-regulation, nuclear architecture, gene regulatory networks, epigenetics, and the genetic basis of complex traits. Drosophila studies also provide insight into the importance of gene-gene interactions and powerful tools to identify genes and pathways relevant to homologous and orthologous traits in humans, gene-environment interactions including interaction between the microbiome and animal physiology, metabolomics and pharmacogenetics, and the characterization of human disease genes. Studies that differentiate cell-autonomous versus non-cell autonomous effects, especially those addressing systemic inputs into cell behavior, are routine in Drosophila, whereas they remain challenging in other animal models, organoids and other ex vivo models. For example, many of the components of signaling pathways that cells use to communicate with each other, including Notch, Wnt, Hedgehog, Dpp, receptor tyrosine kinases, Hippo, and Toll, were first discovered and characterized in Drosophila. Mutations in genes in these pathways are now recognized as central contributing factors to major human diseases including cancer, cardiovascular disease, developmental disorders and neurological disorders. Drugs targeting these pathways are in use or in clinical trials today, with current Drosophila research helping to identify new drug targets. Drosophila research has led to unexpected discoveries about human disease and animal biology, such as insights about human basal cell carcinoma based on knowledge

gained from studying *Drosophila* embryonic patterning genes. Therefore, *Drosophila* research provides an essential pipeline for discovery of drug targets and, in some cases, direct identification of drug candidates and drugs. More recently, *Drosophila* screens have been used for personalized human medicine, where the most efficacious drug regimen can be identified for a patient based on tests in *Drosophila* of the effects of disease-specific mutations from the patient. *Drosophila* thus serves as an outstanding model organism for understanding animal biology and modeling human disease, including identifying molecular mechanisms and new therapeutic strategies.

*D. melanogaster's* was the second animal genome ever fully sequenced and the first animal genome completed by whole genome shotgun sequencing, which was the approach later used for the human genome sequencing. The experimental and computational approaches used in that effort helped guide the trajectory of other genome projects that consequently moved forward rapidly. There are now hundreds of different *D. melanogaster* strains with fully sequenced genomes, providing resources for research on natural variation, population- and quantitative-genetics, areas that have greatly expanded in scope with the reduced cost of genome sequencing. In addition, the genus *Drosophila* – with a known phylogeny, including several species that have been characterized for different biological traits, 108 species with sequenced genomes, and increasing amenability to genetic manipulation – has been a key model for understanding variation and conservation. Comparative genomics studies across *Drosophila* species have elucidated molecular contributors of speciation and evolution, which helped to identify important genomic elements that are highly conserved. Studies across *D. melanogaster* strains performed using the *Drosophila* Genetics Reference Panel have elucidated the extent and consequences of natural sequence variation within species. This, in turn, has guided the best approaches for human genome-wide-association-studies (GWAS) that seek to understand individual human differences, including disease susceptibility and drug-sensitivity/effectiveness. *Drosophila* also serves as the closest genetic model for the major insect vectors of disease, including *Anopheles gambiae* (malaria), *Aedes aegypti* (zika, dengue fever, yellow fever), and *Culex pipiens* (West Nile fever). Understanding medically and agriculturally important insects has been facilitated by *Drosophila* research, including pollinators such as honeybees and pests that include many species of Diptera (for example, Tephritids and *Drosophila suzukii*), beetles and aphids. The enormous contributions of *Drosophila* research have been acknowledged in part through recognition of many *Drosophila* researchers with major scientific prizes, including six Nobel prizes awarded to ten researchers.

*Drosophila* offers a unique and overwhelming combination of strengths as an experimental model. *Drosophila* research is facilitated by a vigorous and collaborative community of researchers, relatively low fly-maintenance costs, short generation time, and a relatively simple genome that can be readily engineered for molecular-genetic studies. The *Drosophila* research community has built an extensive and accessible research toolkit that provides diverse strategies for manipulation and visualization of gene/protein functions; cells, stock-centers and curated online resources; and detailed databases of gene and protein-expression at the tissue, stage, and single-cell level. Recently, a complete map of the adult brain connectome at electron microscopy resolution and a single-nucleus transcriptomic atlas of the adult fruit fly were completed. The entrenched tradition in the community that cutting-edge resources are made readily available to all researchers has greatly facilitated progress for all biomedical and animal research. The unique position of *Drosophila* as a biologically complex, yet easily manipulated and analyzed, animal model makes it especially well-suited for a broad range of studies.

*D. melanogaster* has also been widely used for educational outreach and training. In pre-college classrooms, *D. melanogaster* is an accessible, simple and safe model system to introduce children to experimental science, which is critical for sparking scientific interest. In college classrooms, *D. melanogaster* has long been an important mainstay for introducing a broad range of genetic and developmental biology concepts. Importantly, classroom laboratory exercises that teach sophisticated biological concepts can be performed without the use of vertebrate animals. Drosophila community members have shared laboratory exercises that use readily obtainable Drosophila strains. Scholars earning their PhD or conducting post-doctoral research using Drosophila as a model are trained in a broad range of experimental, computational and theoretical biology areas. The expertise gained by these trainees enables them to contribute in diverse and important professional settings.

## **Part II: Maximizing resources for Drosophila research**

The ability of Drosophila research to continue to pioneer our understanding of general principles underlying the biology of animals, including humans, depends both on the availability of funding and on continual reassessment of and investment in the resources necessary to support Drosophila research. We strongly emphasize the need for continued funding of investigator-initiated research into both basic and applied problems in biological sciences, for instance through the NIH R01 or R35 mechanisms. Such research, in turn, requires continued and robust support of community resources (databases, stock centers, etc.). We also encourage better integration of Drosophila researchers during the planning stages of larger projects, much like our community's participation in the Drosophila Genome Sequencing Project led by the Berkeley Drosophila Genome Project, NIH/ NHGRI ENCODE, NIH/ NHGRI modENCODE and NIH/ NHGRI ModERN projects. We strongly emphasize the need for continued and increased support of these shared resources that serve as the foundation of the Drosophila research community as outlined in this document. Here, we outline current resource priorities of the Drosophila research community.

### **1) Database and informatics resources for Drosophila research**

To ensure that Drosophila research continues to effectively play a leading role in biomedical and animal research, it is crucial to have a central database resource that captures, organizes and presents core information on Drosophila. The primary resource for such information is [Flybase](#), which is invaluable to the Drosophila community, as well as non-Drosophila researchers, and educators. High quality literature curation is one of the features that makes FlyBase a unique and highly valued resource. Such expert literature curation cannot be automated. There is universal agreement within the Drosophila community that continued support for the Flybase curated database is essential to all Drosophila research. The Flybase portal provides search tools and links that allow one to access information at different levels. One of the most widely used tools is for acquiring information about a specific gene of interest. Flybase provides a range of critical information on each Drosophila gene page that helps research move forward efficiently. This information includes a summary of the function of the gene, up-to-date gene annotations, characterization of mutant phenotypes in different tissues/organs, RNA and protein expression profiles, Drosophila stocks/mutant alleles and molecular reagents, links to orthologs/homologs in other species, as well as many other types of information that are annotated in detail on the gene page. The page greatly simplifies the process of identifying the reagents that are available to study that gene and the sources from which they can be obtained. There are also key bioinformatics resources that are linked to each gene page, including genomic-scale resources such as genome and transcriptome sequence information, protein sequence

information, and protein structure prediction including AlphaFold. Additionally, gene expression information is provided from different developmental stages and tissues, including the results of RNA-sequence analysis and single-cell RNA-sequencing. Flybase offers several additional query tools to provide efficient access to the available data and to facilitate the discovery of significant relationships between genes, proteins, and phenotypes. For example, a Parkinson's Disease "Human Disease Query" yields the names of Drosophila homologs of genes implicated in Parkinson's Disease along with the information from Drosophila research on Parkinson's Disease. Another example is the ability to search for all Drosophila Transcription Factors or sub-classes of Transcription Factors, by performing a "Gene Groups Query". The ability to access Drosophila data at such different levels is critical for making connections across disparate bodies of information and accelerating scientific discovery. The Flybase portal provides access to large-scale datasets including whole genome sequences, full RNA-seq data sets, and focused BLAST searches. The Flybase homepage also serves as a community page for announcements, educational outreach, and links for multi-species mining, among many resources. Whereas capture of some classes of information from the literature may be automated, organizing and presenting most classes of information requires manual curation. Furthermore, all data classes require community input, direction and oversight. Non-specific or all-purpose genetics and genomics databases are not a viable substitute for Flybase.

To enhance the accessibility and utility of Drosophila database resources for Drosophila researchers and for those working with other systems, it is essential to link resources dedicated to Drosophila with those dedicated to other organisms. Linking FlyBase and external databases provides opportunities for further exploration to gain insights about connections to human disease, and additional resources of biological and molecular information to understand animal biology. Altogether, it is essential that the unique classes of information fundamental to Drosophila research be preserved and enhanced so that these databases will continue to benefit future research. Over the years, FlyBase has matured from a database to a knowledgebase (for example see [Larkin et al., 2021](#)). We strongly support FlyBase's current efforts to continue to curate the Drosophila literature and reagents. It is also essential to improve the utility of Flybase for colleagues in the human genetics/population-genetics and other model organism communities to maximize discovery. In the future it is important that Flybase continues to curate and integrate relevant and emerging data sets, and to develop tools that enable better access to this wealth of data. Flybase should facilitate more integrative analyses and bioinformatic approaches, specifically for the exploration of transcriptomic, proteomic and other large data sets. We support FlyBase's future plans to more rapidly and effectively curate and disseminate genetic and genomic data to benefit the rapidly changing scientific data landscape. We also support the continued contribution of Flybase to the Alliance of Genome Resources (the "Alliance") in harmonizing and integrating model organism databases (MODs), so long as these efforts do not interfere with or distract from the unique features of Flybase that are so critical to the Drosophila community. Flybase should also continue to improve two-way interactions with the community through outreach and feedback, which has already led to improvements in Flybase utilities. We also applaud FlyBase's effort to support the use of Drosophila as a classroom and outreach teaching tool. Given the importance of Flybase to all Drosophila researchers, a separate White Paper has been generated that provides more detail specific to Flybase.

We are seriously concerned about the absence of coordination of NIH policies on database support and the lack of national and international efforts to support FlyBase. In the past, most funding for FlyBase has come from a large grant from the National Human Genome Research Institute

(NHGRI) and a smaller grant from the UK Medical Research Council. This situation changed in 2016 when NHGRI decided to reduce FlyBase support, in an effort to promote the Alliance. The projected budget for FlyBase's final year of the current 5-year grant cycle and for its next renewal in 2023 will be 50% of what it was in 2016. Additional funds for FlyBase are presently provided by an NHGRI supplement for the Alliance and an NSF grant, which altogether will bring FlyBase's funding closer to 60-65% of its 2016 funding. It is expected that funding needs will be greater in the future given the increased curation necessary with the expanding number of genomic, proteomic and metabolomic data sets, for example. In addition, development of new query tools will be important so the rich dataset resources can be fully explored. Efforts to explore mechanisms that would bring in more international funding have so far been unsuccessful. The Drosophila community has responded well to the request by FlyBase for annual usage fee contributions, but these amount to approximately 5% of the current FlyBase needs. Community contributions will not solve the funding deficit. A 2021 letter from Fly Board presidents (past, current and future) to solicit help from the NIH Director and Directors of five Institutes (NICHD, NHGRI, NINDS, NIGMS and NIDDK) did not lead to additional funding opportunities. We support the plan by FlyBase organizers to seek face-to-face meetings with the NIH Institute Directors to discuss Flybase's critical support needs and how to meet them.

## **2) Resources for analysis of genes and phenotypes**

Resources that facilitate functional analysis of genes and elucidation of mutant phenotypes are a high priority for Drosophila researchers. Gene expression databases such as [BDGP in situ homepage](#), [FlyFISH](#) and [FlyLight](#) provide initial insights into gene function. A powerful advantage of Drosophila as a model system lies in the wide repertoire of genetic manipulations that are possible with this organism. In North America, efforts to generate large strain collections have recently been accomplished by consortia including: the [Gene Disruption Project](#) at Baylor (led by Hugo Bellen), the [DRSC/TRIP Functional Genomics Resources](#) at Harvard (led by Norbert Perrimon), and the [FlyLight Project](#) (Janelia). The continued enhancement of this genetic toolkit should include expanding the set of genes with loss-of-function mutations, including null alleles created by gene deletion or disruption, and resources that facilitate replacement of genomic loci with allelic variants. CRISPR/Cas9 technology makes it possible to target any gene. An expanded collection of mutations that covers most or all genes, including genes without large ORFs (encoding peptides or small RNAs) and hence underrepresented in existing gene disruption collections, will be a valuable resource. Development of genetic resources should advance strategies for manipulating the activity and expression of genes with tight spatial and temporal control, including expression of wild-type or variant alleles, optogenetic methods, and strategies that enable targeted knock-out or knock-down of gene expression through transgenic RNAi, CRISPR/Cas9 and its derivatives, or protein degradation. The continued development of systems for spatial and temporal manipulation of expression (e.g. GAL4, LexA, QF, MIMIC/CRIMIC, MARCM, regulatable GAL4s such as tet-on, split-Gal4, etc.) will also be critical. Together, these will allow for conditional and reversible removal of genes, mRNA or proteins with exquisite precision. Insertional alleles created by targeting GAL4/LexA/QF to recapitulate gene expression, and/or knock down gene function, combined with expression of cDNAs under GAL4/LexA/QF control, will enable proper spatial and temporal expression for rescue experiments, including expressing altered genes for structure-function studies and following developmental histories using lineage tracers such as G-Trace and FlyBow. These tools can also be used for expressing tagged proteins for analysis of protein localization, expressing reagents for cell-type specific genomic studies, expressing genes to manipulate physiology, and expressing homologous genes from humans or other species, among many approaches.

We support continued development of tools to study human genes and their disease variants using *Drosophila*, facilitating emerging strategies in precision medicine, and accelerating characterization of rare diseases, or diseases for which little is known about the biological mechanisms. Creation of a library of human cDNAs in fly-ready vectors allows all researchers to quickly obtain, modify and study human genes. In addition, we advocate for creation of a collection of transgenic fly stocks that carry tagged UAS-human cDNAs. This will permit rapidly testing the function of human genes in *Drosophila* and provide a basis for the functional testing of different human disease alleles/variants, an increasingly common need in medical genomics. We support efforts to provide collections of mutants for genes that have homology to human disease genes.

We advocate support of community facilities and resources for high-throughput screening, including RNAi or CRISPR/Cas9-based screening, and pharmacological screening, both in cell lines and in whole animals. Efforts such as these have already been initiated at [DRSC/TRiP](#) Functional Genomics Resources at Harvard. While the ability to analyze genes and phenotypes *in vivo*, in an intact animal, is a particular strength of *Drosophila*, some classes of experiments can be more easily performed on cultured cells. Expanding the collection of *Drosophila* cell lines available at the DGRC to include more diverse cell and tissue types and improving on methods to culture cells and tissues *in vitro* will facilitate live imaging studies and biochemical and pharmacological characterization and screening of cells and tissues.

We advocate for resources that enable, enhance, and expand physiological and phenotypic characterization of *Drosophila*. These will provide a deeper understanding of responses to environmental perturbations, gene-environment interactions, and polygenic traits. This should include determination and annotation of the *Drosophila* metabolome, and the establishment of standardized protocols and resources to permit comparisons of the metabolome across tissues, genotypes, and species. It should also include analysis of the *Drosophila* microbiome and its contribution to physiology, including resources to characterize microbiomes in diverse *Drosophila* genetic backgrounds and environments. It is clear that translational control adds another layer to gene expression regulation. Therefore, we support the expansion of proteomic studies and generation of proteome datasets across cell types, tissues and developmental stages (for example, [Casas-Vila et al., 2017](#) and [Fabre et al., 2019](#)). We support the efforts to profile the translational landscape under different conditions, for example with ribosome profiling studies using tagged ribosomal subunits.

Tools and resources to determine the expression patterns of *Drosophila* RNAs and proteins at high temporal and spatial resolution, together with sub-cellular localization profiles, provide essential insights into function and valuable markers for phenotypic characterization. To extend the expression analysis toolkit, we advocate two complementary approaches: the creation of collections of tagged genes and the production of antibodies/nanobodies against *Drosophila* proteins. Antibodies are a foundational resource in molecular biology, as they enable the study of protein localization, modifications, and interactions, *in situ*, with genes under endogenous regulatory controls, without any potential for impairment of gene function by tags. A repository of highly specific, high affinity, and sustainable antibodies will be a valuable resource. And in addition to immunization, synthetic techniques including recombinant antibodies, nucleic acid aptamers and non-immunoglobulin protein scaffolds and genetically encoded nanobodies should be expanded. Through the use of CRISPR/Cas9 strategies it is now also possible to create strain collections that express epitope-

tagged proteins, which facilitate rapidly understanding protein localization and protein functions. Tags are needed as an efficient, reliable, and inexpensive way to study protein localization, characterize protein function and to perform immunoprecipitation analyses to understand protein-protein interactions, given current limitations of antibody resources. Limited sets of tagged genes are currently available, but broader gene sets need to be generated, along with stable fly lines expressing them. The activity of tagged proteins needs to be confirmed by genetic experiments. These collections should include tagging endogenous genes with markers (e.g., GFP, Flag, V5, and split-GFP for intersectional strategies) at their genomic loci, without disrupting gene function, to assess expression patterns of genes and subcellular localization of proteins in wild-type and mutant backgrounds and provide reagents for approaches like tag-based knock-down or immunoprecipitation experiments. Collections of transgenes that express tagged cDNAs (e.g., UAS-cDNA-tag) can also be used for localization and interaction studies and are valuable for structure-function studies and comparisons to human UAS-cDNA collections. Many genes produce multiple transcript isoforms via alternative promoter use or alternative RNA processing, including regulated alternative splicing; future analysis of expression patterns should include the spatial and temporal distribution of alternative transcripts and protein isoforms.

Support for functional analysis of the *Drosophila* genes and phenotypes must be coupled to Flybase curation efforts that will establish atlases and databases of the resulting data sets, and make them accessible to all researchers, as described above in the Database and Informatics Resources for *Drosophila* Research section. It must also be coupled to mechanisms for making tools and resources widely available, as described below in parts 3 and 4.

### **3) *Drosophila* stock centers**

Stock centers that provide universal access to genetically defined stocks are essential for all *Drosophila* research and teaching efforts, and they remain a high priority for infrastructure funding. These are complex operations that are heavily used by the national and international fly communities. For example, the Bloomington *Drosophila* Stock Center ([BDSC](#)), the NIH-funded repository for *Drosophila melanogaster* strains, maintains more than 78,000 genetically distinct stocks and distributes approximately 215,000 samples to 2,000 laboratories every year. Distributed stocks include classical alleles, GAL4, split-GAL4 and other driver lines, lines for RNAi of particular genes, marked and balancer chromosomes, species reference-lines, etc. In another example, the National *Drosophila* Species Stock Center ([NDSSC](#)), houses over 250 *Drosophila* species, maintaining approximately 1600 stocks. These stock centers, whether general or specialized in scope, distribute the “core” stocks necessary for genetic experimentation in *Drosophila*. The North American *Drosophila* Board also supports the efforts of our colleagues in other countries that maintain additional centers that distribute other *Drosophila* stocks.

Stock centers must have the physical ability to maintain the large number and variety of stocks needed for contemporary genetics research in a safe and reliable manner. To retain relevance and impact, they also need the management capacity to assure that the collection contents adjust to changing research needs. Stock centers must keep valuable existing stocks while acquiring new stocks from researchers and integrating with or leading large-scale resource development projects. To maximize the benefit of maintaining the strains, stock centers must provide information that will promote their experimental use by integrating stock information into online model organism databases such as FlyBase, emphasizing website development and maintenance, and having staff available for

consultation. These efforts to provide information on stock applications are particularly important to investigators new to *Drosophila* research, such as those wishing to pursue discoveries made in vertebrates using the sophisticated genetic approaches available in flies. Stock centers must also have the capacity to deal with regulatory challenges associated with the distribution of live animals and with the administrative challenges of acquiring large proportions of operating budgets from user fees.

We strongly believe that healthy partnerships between stock centers and funding agencies will continue to be a key factor for the continued success of *Drosophila* as a leading research organism. We urge funding agencies to recognize that the viability and vitality of stock centers depend on both healthy grant support and user-generated income, and that the balance between these funding sources needs to be continually reevaluated based on emerging technologies and the needs of researchers. Cost-recovery programs have enabled stock centers to expand beyond the limits of grant funding and they have contributed enormously to the financial stability and security of these facilities. Nevertheless, both stock centers and funding agencies are constrained in meeting the needs of the *Drosophila* research community by policies that mandate that ever-increasing proportions of operating costs come from user fees and that strictly limit the amount grants can increase upon renewal. Given the increasing relevance of *Drosophila* research to biomedicine, we argue that increased federal investment in *Drosophila* stock resources is not only appropriate and necessary but also advantageous for the broader biomedical research endeavor.

#### **4) Genomics resources**

In addition to a repository for live *Drosophila* stocks, it is important to maintain reliable, central repositories and centers that generate and distribute key reagents to the scientific community expeditiously, as this can relieve individual labs of this responsibility and afford the end user a dependable timeline for receiving materials. Central repositories also ensures that all community members have access to standardized resources, that these valuable resources are not degraded or lost, for instance when labs close down, and provides technical guidance and ready access to reliable, relevant protocols. The importance of molecular stock centers is magnified by NIH and journal guidelines that emphasize reproducibility and require investigators to make materials widely available.

We continue to support the efforts of the Berkeley *Drosophila* Genome Project ([BDGP](#)), including their efforts in genome sequencing, cDNA library preparations, and genome annotation. We continue to support the efforts of the *Drosophila* RNAi Screening Center ([DRSC](#)) to generate and distribute resources for gene manipulation such as TRiP RNAi and CRISPR stocks, as well as to continue to develop new technologies, modified cell lines and reagents for RNAi and CRISPR cell screening, and to continue to disseminate technological know-how and provide practical training on new technologies through a variety of mechanisms. We applaud efforts by individual labs that have produced valuable community resources such as FlyCRISPR, *Drosophila* Genetic Reference Panel, and *Drosophila* Synthetic Population Resource. We acknowledge similar efforts by centers and groups outside of North America.

We continue to support the *Drosophila* community-run genomics/molecular stock center called the *Drosophila* Genomics Resource Center ([DGRC](#)). First and foremost, a molecular stock center needs to be able to accept both resources generated by large-scale projects, as well as donations from



individual labs. The DGRC is the NIH central repository that provides the community with access to an expanding set of key molecular and cell-line resources at affordable costs. As such, this central repository enhances research capabilities, enables efficient use of resources, and facilitates exchange of materials.

New critical resources are being created continually. Currently, key resources being maintained and distributed include germline transformation vectors, as well as collections of full-length cDNA and genomic clones in appropriate vectors for expression in flies, in cell lines, and in yeast or bacteria. Molecular reagents for manipulation of gene expression (e.g., by RNAi or CRISPR/Cas9) as well as the numerous *Drosophila* cell lines also need to be maintained and distributed. Support for antibody repositories is also invaluable. Some *Drosophila* monoclonal antibodies are available from the NIH-supported Developmental Studies Hybridoma Bank ([DSHB](#)), but in the future, support for storage and distribution of polyclonal antisera, and antibody reagents created by other techniques such as phage display, would also be advantageous.

### **5) Long-term preservation of *Drosophila* strains**

Unlike the strains of most other genetic model organisms, *Drosophila* strains presently cannot be maintained practically in any form other than living cultures. The development of robust methods for the long-term preservation of *Drosophila* strains would benefit biomedical research by providing more options for maintaining and distributing strains, allowing the preservation of important, but rarely used strains, preventing the accumulation of mutations associated with long-term culture, and helping to secure genetic resources from disaster. Recent advances in cryogenics and dehydration technologies, and nutritional and environmental manipulations suggest that new methods for long-term preservation could be developed for *Drosophila* embryos, larvae or sperm. We welcome the [2021 publication](#) reporting success in cryopreservation of *Drosophila* embryos and encourage funding agencies to dedicate funds for scaling up cryopreservation from proof-of-principle to high-throughput. In general, we strongly support investing in the development and application of methods that hold promise.

In summary, *Drosophila* research has made tremendous contributions to biomedicine and will continue to do so with continued support and funding. We hope that information communicated in this document will help the *Drosophila* research community, funding agencies and external decisions makers in making sure this happens.