GenTaR User Manual

Date: 2021-08-04

Introduction

GenTaR is designed as a system to enable users to track the production and phenotyping of different types of mutant allele for both CRISPR and ES Cell based experiments, and to coordinate this work with other production and phenotyping facilities to avoid duplication of effort. GenTaR is also designed to allow consortia, which are groups not directly involved in the work tracked in GenTaR, such as a network of clinicians, to follow the progress made in characterising a set of genes that they are interested in.

GenTaR is a modular system that consists of an Application Programming Interface or API, which controls access to information stored in a database, and a web interface that is built on top of the API. The website is available under the URL

https://www.gentar.org/tracker/

The user interface provides a convenient way of interacting with the data stored in the GenTaR database. This user manual outlines how to use the web interface. If you are interested in bulk data access please see the documentation on the GenTaR API under the following URL
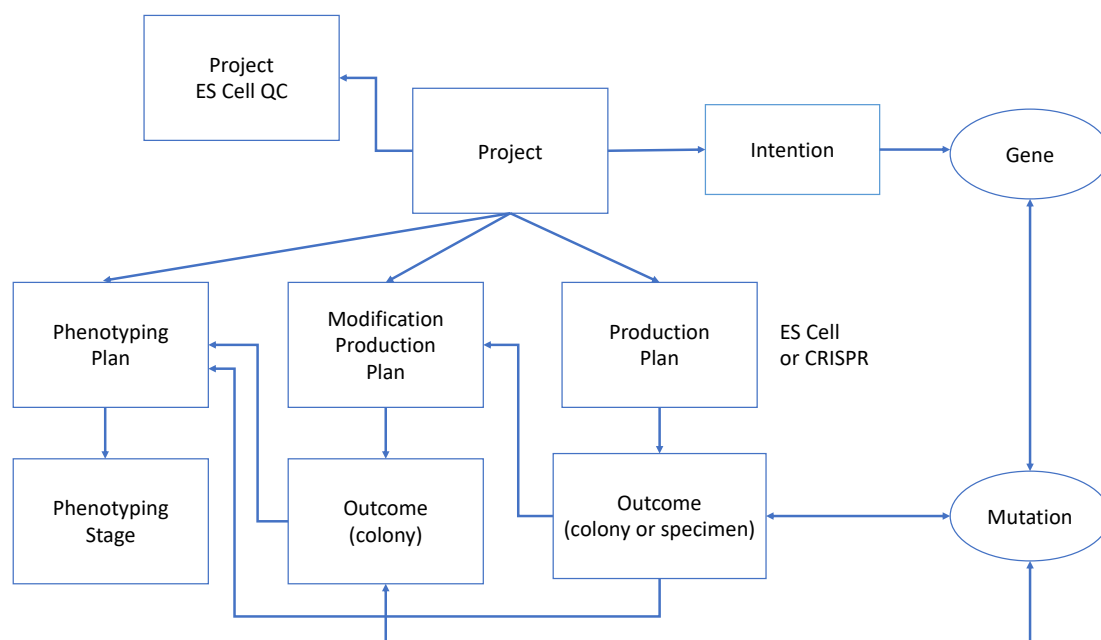
https://www.gentar.org/tracker-api/docs/restapi.html

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An overview of GenTaR

GenTaR is organized according to projects. Each project has one or more intentions describing the type of mutation and gene targeted. The work carried out within the project is tracked by plans. Production plans record the attempts to produce the mutant, and the results of each attempt are captured as outcomes, which can represent colonies or group of specimens for haplo-essential experiments.

In the case of projects that use ES Cell based gene targeting information if there is information about the checks performed on the ES cells before they are used it will be associated with the project. In addition, for some ES Cell based projects the outcome colony can be modified using the protein Cre. This step is recorded in a Cre allele modification plan and the resulting colony that carries a different allele is considered a separate outcome.
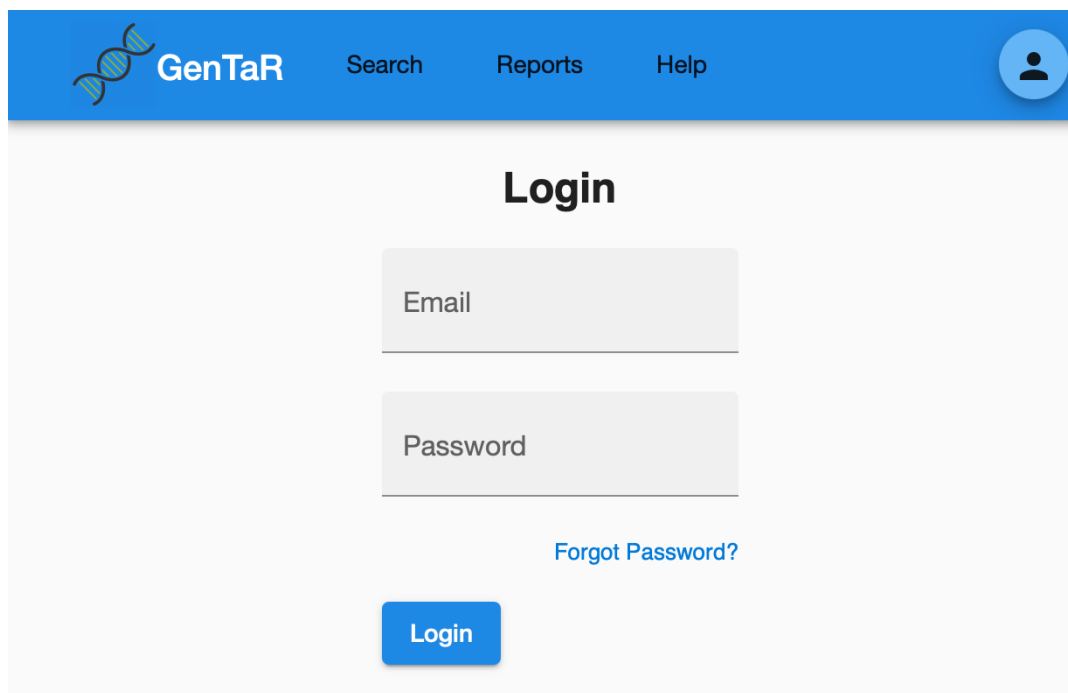
The work carried out to characterize the mutations carried by the resulting colonies or specimens is tracked by the phenotyping plans of the project. Each phenotyping plan can record the independent progress of a number of different phenotyping stages.

Logging into GenTaR

To create a new project or plan, or to view a consortium gene list in GenTaR you need to use your credentials to log into GenTaR. To sign into the application, click on the link that appears when place your mouse over the person icon found at the top right-hand side of a GenTaR page.
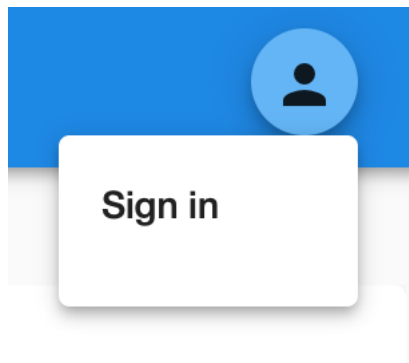
This takes you to a page where you can enter your credentials

To create a project or plan in GenTaR, or to update the information about an existing one, you need to be logged into GenTaR as a user directly affiliated with the workUnit (production centre) that created the plans of the project, whatever the privacy setting of the project. The changes made to a project are tracked and can be viewed from the history links within the site.

Users and Roles

In GenTaR a user can have different roles within the system and be affiliated with multiple consortia or production units. Each user can be a manager for a specific workUnit (production centre), or a general user. It is also possible to have users that are only associated with consortia, and while such users can view information about projects they are not able to edit or update it as this function is restricted to users who have a direct relationship with the workUnit that owns the project or plan. A user who is a manager for a workUnit can also create new general users for that workUnit.

Changing Your Password
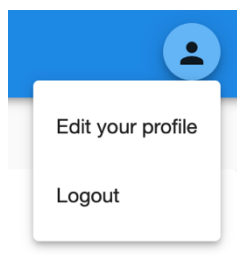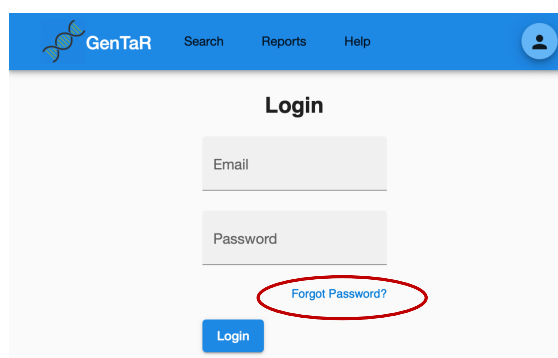
When you are logged into GenTaR as a general user the menu found under the user icon at the right-hand side of the main menu bar provides an option to "Edit your profile"

This link opens a screen which shows the work unit and consortia associated with the account and enables you can change the password used for the account. You can also indicate whether you wish to be contacted by email.

Resetting your password
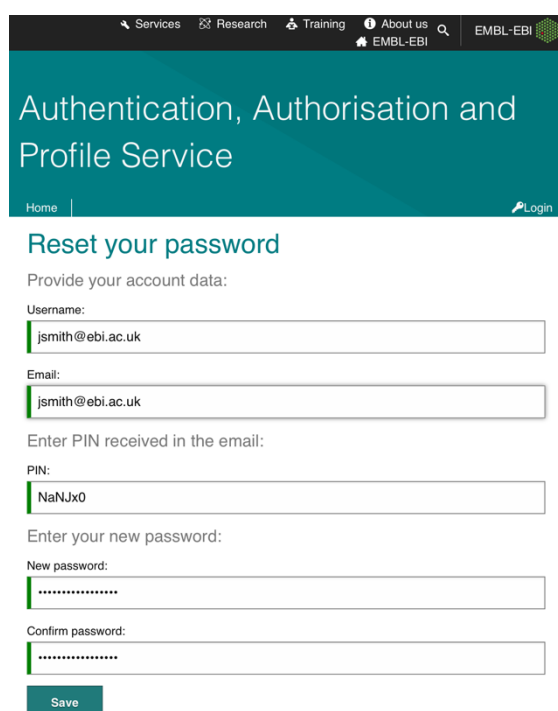
If you are not logged into GenTaR, but already have an account you can also reset your password using the Forgot Password? link on the login page.

This opens a page that asks you to enter your email address. When you press submit an email is sent to this address with a link to a service where you can rest your password and a PIN that is valid for 2 hours.

The external service that allows you to reset your password asks for your username and email. For GenTaR you should enter your email address in both of these fields.

It is important to note that your email address should be provided entirely in lowercase characters, as in the example, which may not be the way you usually format your email address.

User Management
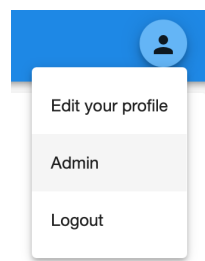
If your account is set up as a manager for a workUnit when you are logged into GenTaR you will have access to an Admin link under the user icon at the right-hand side of the main menu bar.

This gives you access to a page that enables you to create new general user accounts for your workUnit (production centre).

Projects

A GenTaR project tracks all information relating to attempts to produce and phenotype a mutant line. It must contain at least one plan with some minimal information specifying the workUnit (production centre) that created the project. This workUnit owns the project. There can be multiple projects associated with a single gene, some of which may be attempting to produce a point mutations or specific kind of allele rather than the disruption of gene function. In the cases where several projects are created to knock-out the same gene the project assignment status can be useful in coordinating the work among production centres.

Project Assignment Status - Lifecycle and Project Workflow

When a new project is created in GenTaR it will be given an assignment status automatically. This status is aimed at coordinating work for the knock-out project and is based on the state of other projects in GenTaR.

When a new project is created with a single intention specified as a deletion, that aims to target just one gene, the existing gene deletion projects in GenTaR will be examined to see if there is already work related to this gene. The new project will be given the status Assigned if there are no other active projects working on the gene, or one of the Inspect statuses if another project exists.

If the intention of the project is to produce another kind of mutation, such as a point mutation, the project will be given the status Assigned. There is no check to determine if there are other projects aiming to produce a similar mutation.

When all the plans associated with the project are aborted or abandoned, a project transitions into the Inactive assignment state and the date when this occurs is captured. This will cause a reassessment of the assignment status of other projects with a similar intention.

An Inactive project can be activated again by the creation of a new plan, and this state may be transient, such as when a Crispr production plan fails and is aborted before a new plan with details of another attempt is created. However, if a project is in this state for longer than 6 months without any activity the project will transition into the Abandoned state.

When a new plan is created for an Inactive gene knock-out project all other projects in GenTaR that have the same intention are examined before allocating the project a new assignment status. Other types of Inactive project will be given the Assigned status when a new plan is created.

The following is a complete list of the possible assignment statuses for a GenTaR project. Some only apply to ES cell based targeting projects.

Name	Description
Assigned	A workUnit (production centre) has expressed an interest in working on the gene specified in the project intention.
Assigned for ES Cell QC	A work group/work unit has indicated their intention to QC ES Cells
Assigned - ES Cell QC In Progress	The ES cells are currently being evaluated by the production centre
Assigned - ES Cell QC Complete	ES cells have passed the QC phase and are ready for micro-injection
Aborted - ES Cell QC Failed	ES cells have failed the QC phase, and micro-injection cannot proceed
Inspect – Conflict	This gene disruption is already assigned in another planned project
Inspect – Attempt	A gene disruption production plan is already in progress in another project
Inspect - GLT Mouse	A GLT mouse is already recorded in GenTaR for another project that planned to disrupt this gene.
Inactive	All of the plans associated with the project are marked as aborted or abandoned.
Abandoned	This project is marked as abandoned because either the project had been marked as Inactive and no work was performed on it in over 6 months, or because the project was withdrawn by the parties involved. A project in this state can be reactivated, the date when this occurs will be captured.

Project ES Cell QC data

An ES cell based gene targeting project may assess the quality of the ES cells before starting to use them to produce a mutant mouse line. This data is captured as part of the project description. The information captured includes when the ES Cells were received, the number received, which pipeline generated them, the number that started and passed QC. If the ES cells failed QC, a reason for the failure can also be recorded.

Project Privacy

GenTaR permits the specification of a privacy setting for a project. There are three levels within the system: Public, Protected and Restricted. The data access policy chosen for a project determines how others can view the data associated with your project.

The data of a Public project can be viewed by anyone. However, in the case of a Protected project a user must be logged into GenTaR to view information about the project. When a project is marked as Restricted a person logged into GenTaR can see that some work is taking place on that gene, to help coordinate work with other centres, however the detailed information about the project is only accessible to people directly associated with it. A user can be associated with a project either through the workUnit (production centre) that they belong to or as a member of a consortium that is linked to the project.

A project cannot remain Protected or Restricted within system forever. After limited period the Restricted and Protected projects will become public. This embargo period is currently envisaged to be one year.

Project Summary Status

The project summary status reports the summary status of the most 'advanced' active plan within the project, or if all the plans are aborted or abandoned reports the Inactive or Abandoned project assignment state.

The project summary status is determined from a hierarchy of statuses within GenTaR. Each plan associated with a project has a state that is captured as the plan status. The plans themselves may be associated with other items, for example a production plan could be associated with one or more outcome colonies. These related items also have state, and the overall state for a plan and its child objects is captured in the plan summary status. The plan summary statuses for all plans associated with the project, including both production and phenotyping plans, are collated to calculate an overall view of progress for the project and this is reported in the project as the project summary status.

Project Identifier

Each project in GenTaR is given a stable public identifier that can be useful when searching for a specific project or discussing work with colleagues.

The identifier has the prefix 'TPN:' to indicate that it is a GenTaR project and this followed by nine digits, e.g. TPN:000000001

Searching for a project

The GenTaR home page has a Project search box. This enables you to look for projects working on a specific gene by entering the gene symbol or MGI accession Identifier for the gene. You can look several genes at once by entering a comma separated list in the text box, or by uploading a text file in which each symbol or MGI identifier is listed on a separate line.

If you are not logged into GenTaR the search results, which are listed below the search box, will only include public data. If you log into the application search results also include data for Protected and Restricted projects (see the Privacy section above for more information).

Filtering project search data

Clicking on the button 'Show Filters' above the Project Search box opens a panel on the left-hand side of the search box containing a number of different filters that can be used to the refine the search. These filters can be used individually, or if you specify several they will act in combination.

Project search results

The list of projects at the bottom of the page by default shows the public projects, or if you are logged into GenTaR all types of projects within the system.

Project summary	Gene Symbol / Location	MGI	Intention	Best Human ortholog	Work Unit(s)	Work Group(s)	Project Assignment	Summary Status	Privacy	Consortia	Access Status
TPN:000000001	Otog	MGI:1202064	Deletion	OTOG	JAX	JAX	Assigned	Phenotyping Started	public	CMG IMPC	✓
TPN:000000002	Dennd6b	MGI:1916690	Deletion	DENND6B	JAX	JAX	Assigned	Phenotyping Started	public	CMG IMPC	✓
TPN:000000003	Zmym2	MGI:1923257	Deletion	ZMYM2	JAX	JAX	Inspect - Conflict	Genotype Confirmed	public	CMG IMPC	✓
TPN:000000004	Sox9	MGI:98371	Deletion	SOX9	UCD	DTCC	Assigned	Founder Obtained	public	IMPC CMG	✓
TPN:000000005	Cep290	MGI:2384917	Deletion	CEP290	UCD	DTCC	Assigned	Phenotyping Started	public	IMPC CMG	✓

When you search for a gene, the results include some additional columns indicating how your search term maps onto the results. In the example below the search term Krox20 is a synonym for the gene Egr2.

Projects search

Enter marker symbols/MGI accession ids or upload a file with the terms to search:

Krox20   ✕

E.g: MGI:1888496, Atrx, Lbr
or upload a csv file (every search term in a new line)
Choose File   no file selected

[Search]

⬇ Download as CSV

Search term	Search Result comments	Project summary	Gene Symbol / Location	MGI	Intention	Best Human ortholog	Work Unit(s)	Work Group(s)	Project Assignment	Summary Status	Colony Name(s)	Phenotyping External Reference(s)	Privacy	Consortia	Access Status
Krox20	Synonym of Egr2	TPN:000001765	Egr2	MGI:95296	Deletion	EGR2	Harwell	MRC	Inactive	Inactive			public	IMPC	✓

Items per page: 20 ▾   1 – 1 of 1   ‹ ›

The columns listed in the results are described below

Name	Description
Search term	The term used in the search
Search Result comments	How the search term maps onto the results
Project summary	Lists the GenTaR identifier for the project and provides a link to a page with a summary of the project.
Gene Symbol/ Location	Contains the current symbol of the intended gene target, or the sequence location associated with the project intention.
MGI	Lists the MGI identifier for the targeted gene. The identifier is linked to the MGI web site.
Intention	The type of mutation specified in the project intention.
Best Human ortholog	The Human gene symbol of the predicted ortholog with most support for the targeted mouse gene.
Work Unit	The production centres involved in the project.
Work Group	The production consortia associated with the project
Project Assignment	This indicates how the project relates to other projects within the system
Summary Status	This indicates the summary status of the most advanced plan associated with the project (see above for a more detailed explanation of how this is determined).
Privacy	The data access policy assigned to the project

Consortia	The organisations and clinical consortia associated with the project
Access Status	This indicates whether you can view all the project information. This column concerns Restricted projects, because when you are logged into GenTaR you can see the gene targeted in this kind of project but may not be able to view the details of the project.

The search results are paginated, and 20 items are returned by default. You can adjust the default number shown by selecting a value from the 'Items per page' drop-down box at the bottom of the page. The arrows adjacent to this box allow you to navigate through the set of results returned.

The results can be downloaded as a CSV file, but for bulk data we recommend using one of the GenTaR report files.

Project Summary

Clicking on the GenTaR project identifier, e.g. TPN:000000001 in the search results takes you to the project summary page with more information about the project.

The top part of the page lists the project identifier, the assignment status, project summary status.

The intention section describes the aim of the project, classifying the mutation in terms of the molecular mutation desired, and any additional categories that apply to the mutation. The intention can be specified in terms of one or more targeted genes, the most common approach, or in terms of sequence location. When sequence is specified, the original unmodified sequence should be provided along with sequence of the desired outcome. Sequence data can be provided in addition to specifying a target gene to fully describe a desired mutation such as point mutation. When sequence data is associated with the project a link entitled sequence details will appear in the sequence information column of the intention section that allows you to view the sequence data for the project.

Below the intention, the data access policy set for the project is shown along with whether the project is recovered from cryopreserved sperm, and the consortia associated with the project. There is also space for comments about the project and notes and comments added on the completion of a project.

The Assignment Status Stamps section, which is closed by default, lists the changes to the project assignment and the date when the status update happened.

At the bottom of the page a summary of all the production and phenotyping plans associated with the project is shown. The attempt type of the plan indicates the kind of

production or phenotyping plan. For an ES cell based targeting project a production plan can be either an ES cell attempt or a Cre mouse allele modification plan.

The plan summary status provides an indication of the how the work specified in each plan is progressing. For more detailed information about the plan and all the outcomes associated with it click on the link 'See plan'.

Production Plans

Plan Details

Plan id:	PIN:0000000001
Summary Status:	Genotype Confirmed
WorkUnit:	JAX
Attempt type:	crispr

See plan

Add Production Plan

Phenotyping Plans

Plan Details

Plan id:	PIN:0000000002
Summary Status:	Phenotyping Started
WorkUnit:	JAX
Attempt type:	adult and embryo phenotyping

See plan

Add Phenotyping Plan

Creating a new project

To create a project, you need to be logged into the system. Once you have entered the system, a 'Projects' heading will appear in the main menu bar and opening this menu will allow you to create a new project.
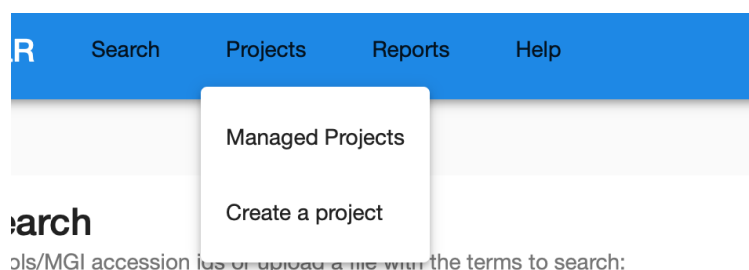
Selecting the item 'Create a project' opens the Project Creation page. This page enables you to associate the project with different consortia that have an interest in the work, for instance a group of clinicians studying the gene. You need to set a privacy setting for the project (see the section on privacy above), which you can select from the drop-down menu by clicking on the downwards arrow. You can indicate whether the project represents a recovery of the line from cryopreserved sperm, either from a public archive or from another IMPC centre. There is some space to add additional comments about the project. You can also indicate whether the project is primarily focused on the study of a mouse gene or a human variant, although this is not required.
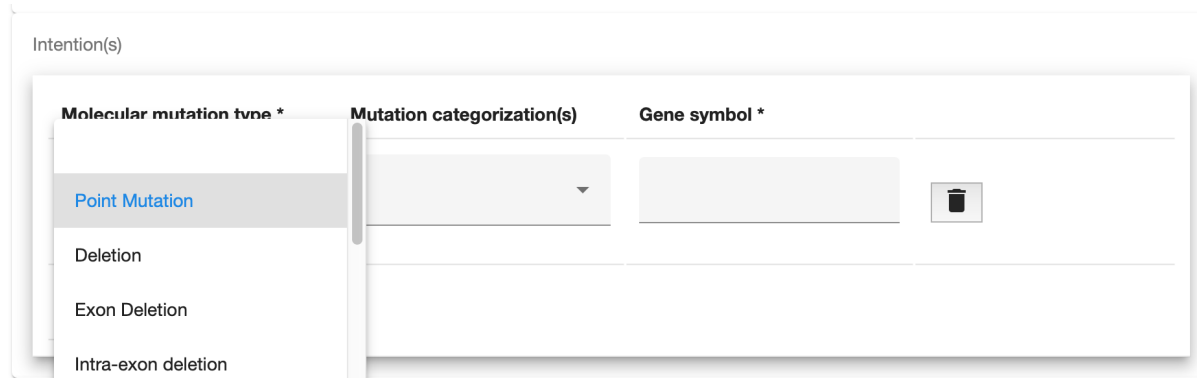
Specifying Project Intention
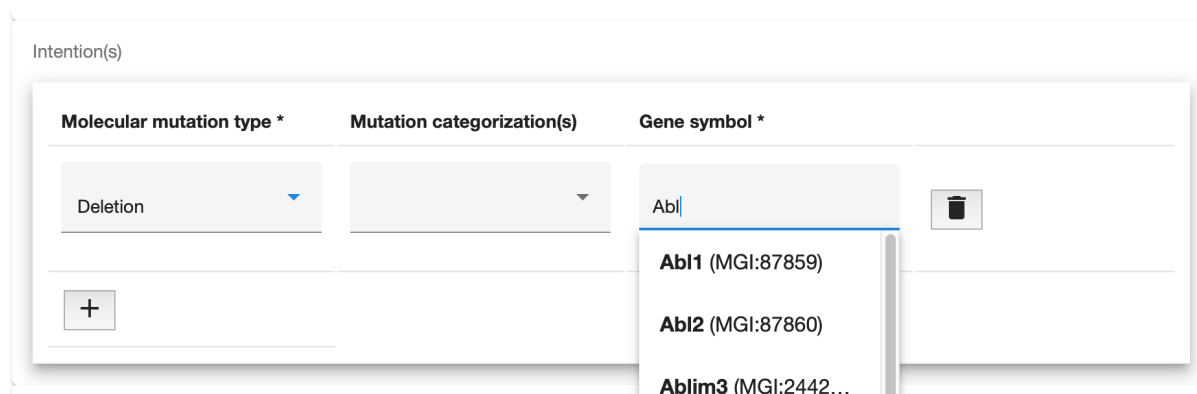
At the moment the aim of the project can be specified in terms of the type of molecular mutation you intend to produce in a gene. As we develop GenTaR we intend to add an option to allow you to specify the project in terms of sequence data describing the targeted mutation you are aiming to introduce.

To specify the aim of project the first step is to click the plus button to add an intention. This enables you to describe a specific intention in term of the type of mutation you wish to create, and the gene you wish to target. You can also assign the project intention to a number of categories, such as 'Null reporter', where those are appropriate.

Once you start typing the symbol of the gene you intend to target a drop-down window will appear with a list of genes, which is refined as you continue to type. Selecting the gene symbol from the drop-down window ensures the gene is specified properly.

If you intend to produce a point mutation and a deletion in the same gene, or create two deletions in different genes, then each of these should be specified as a separate project intention to specify the overall goal of the project.

A project must be associated with at least one plan, that specifies the work-unit (production centre) that created the project. This plan does not need to specify any details about the experimental design, although you can add that information once the project has been created. The minimum information required to specify the initial plan is captured in the Plan Creation section.

Plan Creation

Plan Type *:   production

Attempt Type *:   ▾

Work Unit *:   ▾

Work Group *:   ▾

Funders: ▾

Comment:

Create Project

The initial plan associated with a project is a production plan, in which the attempt type can be specified as either 'es cell', 'crispr' or 'haplo-essential crispr'. The Work Unit, Work Group and Funders drop-downs menus should show the options that are relevant for the user logged into the system. Specification of the Funder is optional, while the Work Unit, Work Group fields are required. There is also space to leave additional remarks about the production plan.

It is important to note that your choices are not captured and entered into the database until you press the button 'Create Project' at the bottom of the page. This button will turn blue once sufficient data has been provided to create a new project.

Editing a Project

To edit an existing project, you need to be logged into GenTaR as a member of the Work Unit that created the project. You can make changes to the project from the Project details page, which you can reach by clicking on the project identifier listed on the search page.

The specification of the project

Once a project has been created the changes you can make to the existing information that defines the project are quite limited. Specifically, you can change the data access policy, and add additional comments, but you cannot change the intention specified as the aim of the project.

However, for projects associated with an 'es cell' production plan you will be able to enter information about the analysis of the ES Cells carried out before starting mouse production.

Es Cell Details:

Order Info

Number Of Es Cells Received:

Es Cell Received From:

Es Cells Received On:

ES Cell QC

Number Of Es Cells Starting
Qc:

Number Of Es Cells Passing
Qc:

Es QC Comment:

After making a change to the project page, it important to press the "Update" button at the bottom of the page to ensure this information is captured in the database.

Adding new plans

You can also create additional plans from the Project Details page to describe new production and phenotyping attempts by using the "Add Production Plan" and "Add Phenotyping Plan" buttons found at the bottom of the page. This is described in more detail below under the section "Creating New Plans".

Managed Projects

When you are logged into GenTaR "Projects" will appear in the main menu bar, and one of the items that is available from this menu is "Managed Projects". Selecting this item shows a list of all the project that are associated with your Work Unit to help you keep track of the projects you work on. You can further refine this list by applying additional filters from the side panel that can be opened by pressing the "Show Filters" button.

Among these filters there are options to search for project using the name of a colony or haplo-essential specimen that has been phenotyped (the Phenotyping External Reference), or the name of an F1 production outcome colony.

≡ Hide Filters

Filter

Clear all ✕

Marker Symbol/ MGI	⌄
TPN	⌄
Colony Name	⌄

Phenotyping External Reference ⌃

JR34017

⬇ Download as CSV

Project Id	Marker Symbol(s)	MGI	Intention	Best Human ortholog	Work Unit(s)	Work Group(s)	Project Assignment	Summary Status	Colony Name	Phenotyping External Reference
TPN:000000003	Zmym2	MGI:1923257	Deletion	ZMYM2	JAX	JAX	Assigned	Phenotyping Started	jr34017	JR34017

Items per page: 20 ⌄ 1 -

Plans

Each GenTaR plan is one part of a project. Plans can represent production or phenotyping attempts, and this is specified when the plan is created. The workUnit (production centre) that started the project can create productions plans within it. Other workUnits are only allowed to create phenotyping plans within the project that track attempts to phenotypes colonies or mutations produced as outcomes of the production plans.

Production Plans

All production plans within the system have the plan type specified as 'production', and the kind of plan is characterised further by the attempt type, which at present can be 'es cell', 'crispr' or 'haplo-essential crispr' or 'cre allele modification'. A 'cre allele modification' production plan relates to an existing 'es cell' production plan, which must have a colony associated with it before the modification plan can be created. As GenTaR develops it will be possible to specify other types of production attempts.

The top section of a production plan contains general information. Each plan has a unique public identifier that has the prefix 'PIN:' to indicate that it is a GenTaR plan followed by ten digits, e.g. PIN:0000000001. The project identifier acts as a link to the project that specifies the intention of this plan. The workUnit and workgroup that created the plan and the funders are also specified in this section.

Plan Details

Project Type:	TPN:000000001
Plan id:	PIN:0000000001
Plan Type:	production
Attempt Type:	crispr
Summary Status:	Genotype Confirmed
Work Unit:	JAX
Work Group:	JAX
Funders:	KOMP2
Comment:	

An ES cell attempt is expected to produce a specific outcome, while a single Crispr attempt could lead to multiple outcomes which may be studied in more detail. The Summary Status captures the highest-ranking status of the plan and any outcomes related to the plan. The state of a successful production plan depends on the plan attempt type, as shown below:

Attempt type	Successful Production Plan Status
Crispr	Founders Obtained
Haplo-essential Crispr	Embryos Obtained
ES cell	Chimeras/Founder Obtained
Cre Allele Modification	Mouse Allele Modification Genotype Confirmed

Each outcome is tracked independently in GenTaR and is also associated with a unique state. The outcome that has the most 'advanced' status, such as a colony that has the status 'Genotype Confirmed' would be reported as the plan summary status rather than outcomes with a lower ranking status, such as colonies with status 'Genotype In Progress' or 'Genotype Not Confirmed', to provide a snapshot of the overall progress of the production plan. In the case of a Cre Allele Modification production plan an outcome colony in the 'Genotype Confirmed' state is required before the modification plan acquires the 'Mouse Allele Modification Genotype Confirmed' status.

The status of the production plan itself is reported under the Status transition section as the

Status transition

Current Status: Founder Obtained

Plan Status History

Status	Date
Plan Created	Feb 26, 2019, 12:00:00 AM
Attempt In Progress	Feb 26, 2019, 12:00:00 AM
Founder Obtained	May 9, 2019, 6:48:00 PM
Embryos Obtained	May 9, 2019, 6:48:00 PM

'Current Status'.
The Plan Status History drop-down section lists the dates when a plan was associated with specific states. Note that these states are just the states associated with the plan, each outcome has a separate history recording when state transitions occurred.

All the possible states for plans and outcomes can be found in the following document:

https://www.gentar.org/tracker-api/docs/state_machine_transitions.pdf

The Production Plan Attempt

The section describing the production plan attempt varies according to the attempt type of the plan. The data entered in the attempt sections is used by GenTaR to automatically assign and update the status of the production plan.

A Crispr production attempt

Production Plan Attempt Experimental Design

The date when the production attempt was performed, and the reference used by the workUnit (production centre) is recorded under the Crispr Attempt Details section. The external reference relating to the mutagenesis information is captured under "Mutagenesis Details" along with the strain used in the experiment

Crispr Attempt Details

MI date:

Tue Feb 26 2019 00:00:00 Gl

MI external Ref:

Otog_118899

Experimental: ☐

Comment:

Mutagenesis Details

Mutagenesis External Ref:

MF-26326

Strain Injected:

C57BL/6NJ

Details about the reagents and the specific concentrations in which they were used for the mutagenesis attempt are recorded in the Guides, Vector/Oligos (mutagenesis donors), Genotype Primers, Nucleases, and Reagents sections. The concentrations are given in ng/µl and if only a single value is shown it applies to all items listed within that section. The Reagents section is currently used to record the addition of the NHEJ Inhibitors Ligase IV or Xrcc5 to the mutagenesis attempt but could include other items in the future.

Nucleases

Type *	Class *	Concentration (ng/µl)
Cas9	protein	250

Guides

Sequence	Guide Sequence	PAM	Coordinates	Strand	Genome Build	Format Name	Source Name	gRNA Concentration (ng/µl)
CTTCACGTACCAAGGAGGGGTGG	CTTCACGTACCAAGGAGGGG	TGG	7:45894563-45894585	+	GRCm39			300
TCTTGCTTCCTACTTCCAGTGGG	TCTTGCTTCCTACTTCCAGT	GGG	7:45895049-45895071	+	GRCm39			

Genotype Primers

Name	Sequence	Start Coordinate	End Coordinate

Vector/Oligos (Mutagenesis Donors)

Oligo Sequence Fasta	Preparation Type	Concentration (ng/µl)

Reagents

Name	Concentration (ng/µl)

The guides section shows the guide and the PAM sequences separately and combined as the sequence used in the experiment. In all cases the sequence are specified in the 5 -> 3' orientation and are provided along with the coordinates and strand for the specified genome build. The guide format can be specified as either 'sgRNA' or 'cr-tracrRNA', and the guide source can be recorded as either 'in-house' or 'commercial'.

Production Plan Attempt Data

The number of embryos injected, the number that survived, and number transferred are recorded under the Crispr Injection Details section:

Crispr Injection Details

Number of Embryos Injected:

59

Number of Embryos Survived:

47

Embryo Transfer Day:

Same Day

Number of Embryos Survived
to 2 cell stage (Leave blank if
transfered on same day):

Number Transfered:

47

The "Founder/G0 Litter" section found at the bottom of the production plan records the number of pups born, and the numbers screened for a mutation and selected for breeding.

Founder/G0 Litter Details

Number of G0 Pups Born:

15

Assay Type Used:

PCR

Number of G0s Assayed:

15

The results of the screen are listed in the G0 Assay Results section. The 'G0 Allele Screen Details' and 'G0 Donor Insertion Details' are drop-down sections that record detailed information about the number of G0 offspring falling into different categories.

G0 Assay Results (Leave fields blank if not tested in your G0 screen)		
Assay results for GENE mutation	Number of G0 with a Detected Mutation:	9
	G0 Allele Screen Details ^	
	Number of G0 with NHEJ Mutation:	
	Number of G0 with Deletion Mutation:	9
	Number of G0 with HR Mutation:	
	Number of G0 with HDR Mutation:	
	G0 Donor Insertion Details ^	
	Number of G0 with All Donors Inserted:	
	Number of G0 with Subset of Donors Inserted:	

An ES Cell Attempt

Production Plan Attempt Data

The ES cell attempt is recorded in four sections.

ES Cell Attempt Details
The ES Cell Attempt Details section displays the name of the ES Cell used in the attempt, the date of the micro-injection (MI date), the reference used to track the experiment in the production centre along with any comments about the attempt.

EsCell Attempt Details

ES Cell Name:	EPD0045_1_B11
MI date:	2010-08-17
MI external Ref:	GSF-EPD0045_1_B11-3
Experimental:	☐
Comments:	

Transfer Details
The blastocyst strain and the number of blastocysts injected, the total transferred and the number of surrogates receiving them are shown in this section.

Transfer Details

Blast Strain Name:	BALB/cAnNCrl
Total Blasts Injected:	59
Total Transferred:	59
Number Surrogates Receiving:	3

Litter Details

Information about the number of pups born in the litters produced by the surrogates is shown in the 'Litter Details' section. This includes the number of offspring that are chimeras for each sex, and data on the degree of chimerism in males.

Litter Details

Total Pups Born:	39
Total Female Chimeras:	0
Total Male Chimeras:	7
Number of Males with 0-39% Chimerism:	0
Number of Males with 40-79% Chimerism:	4
Number of Males with 80-99% Chimerism:	3
Number of Males with 100% Chimerism:	0

Chimera Mating Details

The "Chimera Mating Details' section contains information about breeding the chimeras to produce progeny. It records the test cross strain used, the date the mating was set up, the number of different attempts and the number of successful matings. In addition, this section lists data on the degree of germ-line transmission (GLT) achieved from the chimeras and information about how that was assessed and the date when cassette transmission was verified. The number of het offspring and the number of live GLT offspring are also recorded here.

Chimera Mating Details

Test Cross Strain Name:	C57BL/6NTac ▾
Date Chimeras Mated:	2010-11-02 📅
Number Of Chimera Matings Attempted:	5
Number Of Chimera Matings Successful:	3
Number Of Chimeras With GLT From CCT:	0
Number Of Chimeras With GLT From Genotyping:	1
Number of Chimeras with 0-9% GLT:	0
Number of Chimeras with 10-49% GLT:	0
Number of Chimeras with 50-99% GLT:	0
Number of Chimeras with 100% GLT:	0
Total F1 Mice From Matings:	0
Number Of CCT Offspring:	
Cassette Transmission Verified:	2011-07-13 📅
Number Of HET Offspring:	2
Number Of Live GLT Offspring:	0

A Cre Allele Modification Attempt

A Cre allele modification attempt contains two sections. The 'Original Allele Details' lists the identifiers of the outcome and the ES cell plan that produced the allele used as the starting point for the modification plan, while the 'Allele Modification Details' section contains the reference used by the production centre for the attempt, and information about the Cre modification strategy.

Original Allele Details

Original outcome: TPO:000000008007
Production Plan: PIN:0000020156

Allele Modification Details

Cre Allele Modification external Ref: H-NXN-B11-TM1B

Cre Excision via TAT-Cre?:   ☐

Deleter Strain Name: C57BL/6NTac-Tg(A…   ▼

Number Of Cre Matings Successful: 3

Production Plan Outcomes summary section

The "Production outcomes" section, located at the bottom of a production plan page, lists all the outcomes of the plan. This section summaries the outcomes, listing a unique public identifier assigned to the outcome that has the prefix 'TPO:' followed by 12 digits, the type of the outcome (currently a colony or specimen), the name assigned to the outcome, the background strain and the mutations linked to the outcome if they have been characterized. A specific page with additional information about each outcome is available under the more details link and is described in the Outcomes section below.

Production outcomes

Outcome id:	TPO:000000000001 more details
Type:	Colony
Name:	**jr34077**
Background Strain:	C57BL/6NJ
Mutations:	

Symbol	Molecular Mutation Type
Otog$^{em1(IMPC)J}$	Exon Deletion

Outcomes linked to a Production Plan

An ES cell production attempt is anticipated to produce a single defined outcome, however, potentially a single Crispr mutagenesis attempt could produce multiple outcomes. Each founder animal where a distinct mutation can be identified is treated as a separate outcome that can be bred and tracked as a colony. For haplo-essential Crispr production plans where each embryo obtained could potentially carry a number of mutations, all the embryos produced from the mutagenesis step are treated as a single outcome and tracked as a haplo-essential specimen group that is given a unique reference.

A page for each outcome generated can be accessed from the production plan. The outcome pages track the status of the outcome and this feeds into calculation of the overall summary status of the production plan. The outcome page also has information on the characterization of the mutation produced.

At the top of the outcome page there is a section that has a link back to the production plan. In addition, it displays the public identifier assigned to the outcome, which has the prefix

'TPO:' followed by 12 digits. This section also specifies the type of outcome as a Colony or a Specimen, which is used for the haplo-essential experiments, the background strain and any comments about genotyping.

The status of the outcome is recorded in the next section, and the history of status changes and dates when they occurred are shown in the status history drop down panel. The statuses for colonies and specimen outcomes are quite distinct.

Outcome mutations

Each outcome could be associated with a lesion in one or more genes. The characterization of the mutations identified are recorded within the "Mutations" section of the outcome, at least for colonies produced from a founder animal. In the case of the haplo-essential specimen groups the mutation recorded in this section may represent the ideal mutation, rather than the spectrum of mutations that could be produced. Exactly how this section will be used for haplo-essential data requires further discussion.

Mutations

Mutation id:
MIN:000000000001

Gene(s) *:

Otog

Symbol:

$Otog^{em1(IMPC)J}$

Molecular Mutation Type:

Exon Deletion

Mutation Categorizations:

Repair Mechanism:

NHEJ

Allele Categories:

Each mutation characterized in the outcome is given a separate public identifier that has the prefix 'MIN:' followed by 12 digits. The gene and symbol of the allele or aberration is shown if already assigned. The mutation is also categorized as a type of molecular mutation. This type can take on one of the following values:

 Point Mutation
 Deletion
 Exon Deletion
 Intra-exon deletion
 Inter-exon deletion
 Whole-gene deletion
 Copy Number Variant
 SNP
 Insertion
 Inverted insertion
 Inversion
 Indel
 Complex rearrangement
 Insertion, Intragenic deletion

In some ES cell projects, you may also see the term "legacy" for data imported from iMits. This term is only used when describing the project intention rather than the mutation carried by a specific outcome colony of the project.

Several different types of deletion could be chosen, but this field only takes a single value, so it is best to use the most specific type when characterizing the mutation. The complex rearrangement can be assigned if a large-scale chromosomal rearrangement has been identified as a result of the Crispr mutagenesis experiment.

Within the "Mutation Categorization" section the repair mechanism is recorded as NHEJ, HR or HDR, and the allele can be specified as falling into one or more of the following categories:

Null Reporter
Conditional Ready
Conditional
Conditional point mutation
Cre
Overexpressor
tag knock-in
Bespoke
Cre-Bac
Cre knock-in

Some of these categories are only relevant to mutations derived from ES cells and in the future the list will be tailored according to the attempt type.

Sequence data defining the mutation

The addition of sequence data is one of prerequisites for the transition of a colony to the "Genotype Confirmed" state.

Sequence(s) information

Index	Sequence	Type
1	>Otog TGGGACTAGGTCACAGACAGAAAAAGGGGGATGAGAAGGCCTTAGATCTAAGGGAGGTAAAG AGAGAATTAACCACAGGAATTAGCACACTGAAGGATCGTGCTCGCCAGACCTCAAACCATCTC CTTCTTGCGTCATGAGAAAGCCTTGACCCATCATTTTCCAGTTTTCTGTGTTCTTGCCCCACTT TGGCCCCTGGATCCTGGGATCTCCCCAGAAATTCTTACCTAGCCCC	complete

Sequence data is reported in the FASTA format and each piece of sequence is assigned an index number. A type is used to indicate if the sequence data represents the complete characterization of the mutation, or only a partial characterization of the mutation. In some cases, such as complex rearrangements, more than one piece of sequence may be used to define the breakpoints of the mutations and it may be appropriate to record the sequence as "5_prime_end" or "3_prime_end" sequence. Only one piece of sequence data associated with a mutation should be given these designations, and they imply the sequence data provided does not fully characterize the mutation.

If multiple pieces of sequence are added and all typed as 'complete', there is an assumption that these sequences are contiguous and ordered 5' to 3' in the order specified by the sequence index number.

Note: a sequence box can be expanded to show the complete sequence by dragging on the hatched area in the bottom right-hand corner of the box.

Mutation description and QC

Additional information about the mutation is recorded in the mutation description box and the results of different type of assay used to evaluate the mutation created are reported in the "QC Results" section.

Mutation description:

Otog<em1(IMPC)J>:
This allele was generated at The Jackson Laboratory by electroporating Cas9 protein and 2 guide sequences CTTCACGTACCAAGGAGGGG and TCTTGCTTCCTACTTCCAGT, which resulted in a 520 bp deletion beginning at Chromosome 7 position 46,245,130 bp and ending after 46,245,649 bp (GRCm38/mm10). This mutation deletes ENSMUSE00000204147 (exon 4) and 444 bp of flanking intronic sequence including the splice acceptor and donor and is predicted to cause a change of amino acid sequence after residue 71 and early truncation 34 amino acids later.

QC Results

Type	Status

The list of assays that can be selected includes assays used to evaluate Crispr and ES cell experiments. In the future this list will be generated based the attempt type. When the data is viewed the Mutation QC section only reports the assays actually employed to evaluate the mutation.

five_prime_screen
three_prime_screen
loxp_screen
loss_of_allele
vector_integrity
southern_blot
five_prime_lr_pcr
five_prime_cassette_integrity
tv_backbone_assay
neo_count_qpcr
lacz_count_qpcr
neo_sr_pcr
loa_qpcr
homozygous_loa_sr_pcr
lacz_sr_pcr
mutant_specific_sr_pcr
loxp_confirmation
three_prime_lr_pcr
critical_region_qpcr
loxp_srpcr
loxp_srpcr_and_sequencing

Each of the QC assays reported can be given one of the following statuses

pass
passb
not confirmed
no reads detected
fail

Distribution of Outcome Products

In some cases, the outcome of a production plan is available to the community as either live mice from an established colony or frozen sperm. The products available are shown in the "Distribution Products" section. This records the distribution centre, the kind of product available, the distribution network (MMRRC, CMMR or EMMA) if appropriate, and the period in which the product is 'on the shelf' where that applies.

Distribution Centre	Product Type	Distribution Network	Start Date	End Date
JAX	Live mice			

Distribution Products:

Phenotyping Plans

A phenotyping plan is used to track all the phenotyping carried out on a production outcome by a specific workUnit (phenotyping centre). For example, one plan is used to report the status both early and late adult phenotyping of a colony carried out by a centre. The status of the different kinds of phenotyping performed on the outcome are tracked as phenotyping stages associated with the phenotyping plan.

The top part of a phenotyping plan is similar to a production plan. It describes the type of plan and who created it. The plan is assigned a unique identifier, in the format 'PIN:' followed by 10 digits. The plan type is specified as 'phenotyping', and the attempt-type can either be 'adult and embryo phenotyping' or 'haplo-essential phenotyping'. The attempt type influences what kind of phenotyping stages can be created to track the progress of phenotyping. The project identifier provides a link back to the main project. The phenotyping plan summary status provides an idea of how phenotyping associated with the plan is progressing, but the detail is captured in the phenotyping stages associated with the plan. The way in which this value is calculated is discussed in more detail below. The workUnit records the centre carrying out the phenotyping, and the workGroup captures the production or phenotyping consortia under whose scope the work falls if that is appropriate. The funder field indicates how the work is supported, and there is space for additional comments.

Plan Details

Project id:	TPN:000000001
Plan id:	PIN:0000000002
Plan Type:	phenotyping
Attempt Type:	adult and embryo phenotyping
Summary Status:	Phenotyping Started
Work Unit:	JAX
Work Group:	JAX
Funders:	KOMP2
Comment:	

The status of the phenotyping plan is shown in the status transition section. A phenotyping plan can only be in one of three states: 'Plan Created', 'Plan Abandoned' and 'Phenotyping Plan Aborted'. The information about the state of the phenotyping attempts associated with the plan is captured in the phenotype stages and summarized in the phenotyping plan summary status. The Plan Status History section, which is a drop-down, shows the dates when the phenotyping plan was in a certain state.

Status transition

Current Status: Plan Created

Plan Status History

Status	Date
Plan Created	Aug 11, 2019, 2:36:44 PM

The Phenotyping Plan Summary Status

The summary status integrates the status of the plan and the state of all the underlying phenotype stages into a single value to give an indication of the how phenotyping is progressing. However, the detail is captured in the statuses of the plan and the associated phenotyping stages. Each phenotyping stage state machine has an independent set of statuses. The status "Phenotyping Started" in the early adult state machine and "Late Adult Phenotyping Started" are separate states. When the phenotyping stage statuses are summarised for the phenotyping plan, they are ranked in the order haplo-essential, early adult and embryo, and late adult statuses, and the highest-ranking status is selected as the plan summary status. This is an arbitrary decision but one we needed to take in terms of selecting a single value. It is important to note that any actual phenotyping will always be reported over phenotyping stages that are only registered for phenotyping. For example, if early adult and embryo phenotyping has reached the state of 'Phenotyping Started', and the line has a late adult phenotyping stage in which it has been registered for Late Adult Phenotyping, then the plan summary status will be reported as 'Phenotyping Started'. However, if late adult phenotyping has been started it will be reported over any active early adult and embryo phenotyping status. Another aspect taken into consideration is that when choosing the status to report as the phenotyping plan summary status an aborted phenotyping stage status is always overridden by an active state in another phenotyping stage state machine.

Phenotyping Attempt Details

Phenotyping External Reference
(Colony or Specimen id):   JR34077

Cohort Production Work Unit Name:

                                  JAX

Background Strain:

                                  C57BL/6NJ

Do not count towards completeness: ☐

Starting Point

Outcome: TPO:000000000001

Production Plan: PIN:0000000001

Information about the line or set of embryos analyzed is listed in the 'Phenotyping Attempt Details' section. The reference used to track the phenotyping experiment by the workUnit (phenotyping centre) is captured in the 'External Reference' field. The workUnit that raised the animal for phenotyping is recorded as the 'Cohort Production Work Unit Name' (Generally this is the same as the workUnit of the phenotyping plan, but in some cases the animals may have been raised elsewhere.) In addition, the background strain of the line or set of embryos is recorded. A checkbox enables you to indicate whether the plan should be counted toward completeness. The starting point section specifies the identifiers of the

production plan and the outcome that relate to the phenotyping plan, and link to this information.

At the bottom of the phenotyping plan the phenotyping stages associated with the plan are listed. Each phenotyping stage is assigned a unique identifier with the prefix 'PSN:'. The type of phenotyping tracked by the phenotyping stage is indicated, and its current status. More information about each phenotyping stage can be obtained by clicking on the 'See Phenotyping Stage' link.

Phenotyping Stages

Phenotyping Stage id:	PSN:000000000001
Type:	early adult and embryo
Status:	Phenotyping Started
See Phenotyping Stage	

Phenotyping Stages

Each phenotyping stage has a unique identifier starting with the prefix 'PSN:' which is followed by 12 digits. The summary section at the top of the page also lists the identifier of associated phenotyping plan which acts as a link back to the plan page. The type of the phenotyping stage indicates what kind of phenotyping is being tracked and can have one of the following values: early adult and embryo, late adult, haplo-essential and embryo. The possible values that can be entered depend upon the attempt type of the phenotyping plan. If the attempt-type of the plan is 'adult and embryo phenotyping' then either 'early adult and embryo', or 'late adult' can be chosen as the type of the phenotyping stage. For a plan specified as a haplo-essential attempt the type of an associated phenotyping stage will be either 'haplo-essential' or 'embryo', which is used to track the phenotyping of haplo-essential embryo cultured beyond the 2-cell stage.

The top section of the phenotyping stage page also reports the external reference, that is used by the workUnit (phenotyping centre) to identify the colony or group of specimens phenotyped. In addition, this section captures the date when the phenotyping experiments started, and there is a field called the 'initial data release date' that is set by the CDA to record the first date when some phenotype data associated with this phenotyping plan became visible on the IMPC web site. This date corresponds to the date of the Phenotyping Complete status in iMits.

Phenotyping Stage id:	PSN:000000000001
Phenotyping Plan Id:	PIN:0000000002
Type:	early adult and embryo
Phenotyping External Reference (Colony or Specimen id):	JR34077
Phenotyping Experiments Started:	2020-02-24
Initial Data Release date:	

The status section of the page shows the current status of the phenotyping stage. This is specific to the type of phenotyping being tracked in this stage. The history section records the dates of all the changes in the status of the phenotyping stage.

Current Status: Phenotyping Started

Phenotyping Stage Status History

Status	Date
Phenotyping Registered	Feb 24, 2020, 7:55:33 PM
Phenotyping Started	Feb 24, 2020, 7:55:33 PM

At the bottom of the page the Tissue Distribution Centre section show the material produced from this phenotyping stage that is publicly available. The optional start and end dates can be used to indicate an interval when the material was in stock. The workUnit shows where the material is held. The kind of material available is specified as the material type, typically this is either 'Fixed Tissue' or 'Paraffin-embedded Sections'.

Tissue Distribution Centre

Start Date	End Date	Work Unit	Material Type
Mar 14, 2019		UCD	Fixed Tissue

Creating a New Plan

To add a new plan to an existing project you need to be logged into the system. If you are associated with the work unit that created an existing production plan for the project, you will be able to create a new production or phenotyping plan, otherwise you can only add a plan to phenotype a colony or specimen produced by the project. This may be relevant if you have imported mice from another centre to phenotype.

Creating a new production plan

When the 'Add Production Plan' button at the bottom of a Project Details page is shown in blue you can create a new production plan. Clicking on the button opens the create production plan page where you can specify the attempt type as either a 'crispr', 'es cell' or 'haplo-essential crispr'. A 'cre allele modification' plan can only be specified if it is linked to an existing colony from a 'es cell' production plan.

Plan Creation

Project id:
TPN:000000001

Plan Type *:	production
Attempt Type *:	▼
Work Unit *:	▼
Work Group *:	▼
Funders:	▼
Comment:	

Create Plan

* required fields

The Work Unit, Work Group and Funders capture who will carry out the work and options appropriate to your user should be displayed. Please note that specification of Funders is optional, however entries in the Work Unit and Work Group fields are required to create new plan. You can also enter any additional comments you wish to record.

When you press the "Create Plan" button it will assign the plan and identifier and open the plan page in the editing view where you can add further information to the plan.

Creating a new phenotyping plan

Creating a phenotyping plan is analogous to creating a new production plan. A new phenotyping plan for a project can be created when the 'Add Phenotyping Plan' button is shown in blue on the Project Details page. In this case the attempt type should be specified as 'adult and embryo phenotyping' or 'haplo-essential phenotyping'. For a phenotyping plan you also need to specify the starting point of the plan by selecting a production outcome of the project (colony or specimen) from the drop-down menu.

Plan Creation

Project id: TPN:000000001

Plan Type *: phenotyping

Attempt Type *: adult and embryo phen...

Starting point (Outcome id) *: TPO:000000000001 (jr34077)

Work Unit *:

Work Group *:

Funders:

Comment:

Create Plan
* required fields

Other fields are similar to those of a production plan, and options appropriate to your user should be shown in the drop-down menus. To assign the plan an identifier and complete the process press the 'Create Plan' button. This opens the new phenotyping plan in the editing view.

Editing a Plan

To edit or update an existing plan, you must log in as a user associated with the work unit (the production or phenotyping centre) specified in the plan. The plans for a project are listed at the bottom of the project details page. If you click on the link "See Plan" this will open the plan page in editing mode, provided you are associated with the work unit that created the plan. Once you add additional information or make changes to the page the "Update" button at the bottom of the page will becomes active, turning blue, and it is important to press this button to ensure your changes are recorded in the database.

When you are editing a production plan, there is a button that allows you to create an outcome to associate with the plan, and in a phenotyping plan you can use the "Add Phenotyping Stage" to create a new stage to track a different kind of phenotyping.
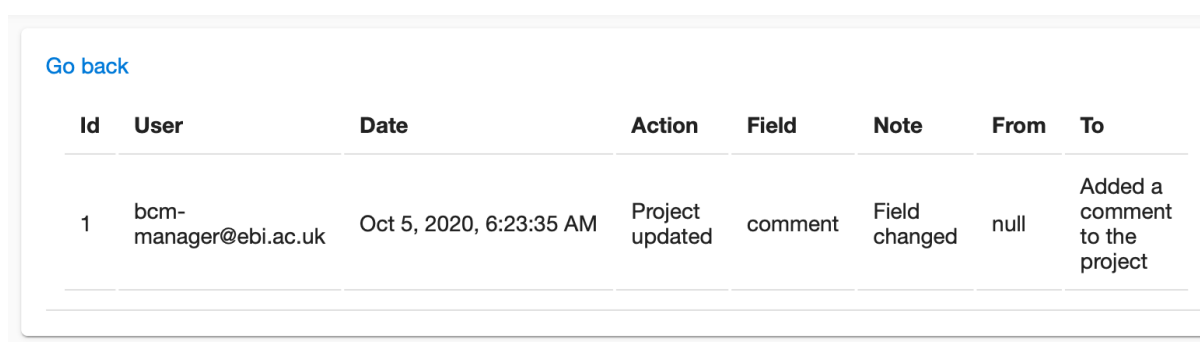
Please note that for a phenotyping plan you cannot add a phenotyping stage until you have entered information about the colony or specimen.

Project and Plan history

You can access the history of changes to a project or a plan from the history link at the top left-hand corner of the screen.
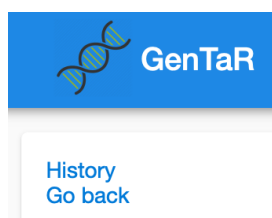
The link opens a page showing the changes that have taken place since the project or plan was created.

Go back

Id	User	Date	Action	Field	Note	From	To
1	bcm-manager@ebi.ac.uk	Oct 5, 2020, 6:23:35 AM	Project updated	comment	Field changed	null	Added a comment to the project

The changes are arranged in chronological order and include a breakdown of the fields that have been changed in the API in order to update the web interface. Please note that the history of changes to the outcomes recorded for production plans, and phenotyping stages associated with phenotyping plans are tracked separately from the main plan, so for example to view the history of changes to a colony you should look at that specific outcome rather than the plan itself.

Glossary

Term	Description
Person	An individual with an account in GenTaR. The individual can be associated with a Work Unit, or a Consortium, or both a Work Unit and a Consortium.
Role	An individual within the system can either be an ordinary user, or a manager for their Work Unit or Consortium. Managers can create other users for their Work Unit or Consortium within the system.
Work Unit	This represents the individual production and phenotyping centres that produce and analyze the mutant mice e.g. Baylor College of Medicine (BCM).
Work Group	A group of production and phenotyping centres collaborating to generate and characterize mutant mice, such as BaSH.
Consortium	A body or organization with an interest in the work, but not actively involved in production or phenotyping. For example, a group of clinicians interested in the human ortholog of the mouse gene.
Funder	A funding body that supports the work of the production and phenotyping centres.
Project	This is the overall entity that collates everything related to the work carried out. The aim of the project is specified an intention such as a point mutation or a deletion.
Plan	The plans associated with a project track the work carried out to meet the goal of the project. Every production and phenotyping attempt is represented by a separate plan.
Status Transitions	Plans, outcomes and phenotyping stages are assigned a state. This status can change depending upon the data entered into the system or through interaction with a user. The possible states that could be adopted given the current status of the entity are shown, and the dates when status transitions happen are recorded.