IMPC phenotyping SOPs in JMC

Viability Primary Screen IMPC_VIA_001

Purpose

To assess the postnatal viability, sub-viability, and lethality of homozygous mice during cohort production.

Description	MP Term
Complete preweaning lethality	MP:0011100
Partial preweaning lethality	MP:0011110

Experimental Design

- Monitor genotypes of Het X Het breeding units; score genotypes of at least 28 pups (if other breeding strategies are used specify in the metadata and follow this convention HomXHet FemaleXMale)
- Definition of female age: "Female age earliest start/Female age oldest end" age of the youngest and oldest female mouse respectively when cohort breeding starts
- Age to be genotyped: P1-P28
- Record sex ratios of pups
- Collect and report all litters and genotype data: flag strains that produce no homozygote pups
- Identify and score lethals (defined as no homozygotes at genotype)
- Identify subviables (defined as <50% of expected homozygotes)
- If homozygous lethal: perform the embryonic lethal pipeline (if available)

Procedure

1. Monitor pup number, genotypes and sex ratios of Het X Het intercrosses set to generate cohorts for phenotyping. Score at least 28 pups when genotyped.
2. Identify strains that produce no homozygous/hemizygous male or female pups.
   a. Strains that produce NO homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
   b. X-linked strains that produce NO hemizygous male pups and NO female homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
   c. These will undergo embryonic lethal pipeline (if available)
3. Identify strains that produce less than normal numbers of homozygous/hemizygous male or female pups.
   a. Strains that produce <50% expected (#totalpups * 0.125 (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) homozygous pups will be considered SUBVIABLE (partial preweaning lethality [MP: 0011110]).
   b. X-linked strains that produce <50% expected (#total pups* 0.125 (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) hemizygous male pups and female homozygous pups will be considered SUBVIABLE (partial preweaning lethality [MP: 0011110]).
   c. Some centers will proceed with secondary screening.

4. For lethal and subviable strains, heterozygous progeny will be sent for adult phenotyping.

Notes

All genotypes should be collected using validated assays.

Line level calls will be rejected until 28 mice have been genotyped.

Sub-viable significance table:

Number genotyped	Pups observed	Formula (Excel)	P-value
28	3	=BINOMDIST(3,28,0.25,1)	0.055135567
29	4	=BINOMDIST(4,29,0.25,1)	0.115324345
30	4	=BINOMDIST(4,30,0.25,1)	0.0978696
31	4	=BINOMDIST(4,31,0.25,1)	0.082764531
32	4	=BINOMDIST(4,32,0.25,1)	0.069757389
33	4	=BINOMDIST(4,33,0.25,1)	0.05860841
34	4	=BINOMDIST(4,34,0.25,1)	0.049093333
35	4	=BINOMDIST(4,35,0.25,1)	0.041005517
36	4	=BINOMDIST(4,36,0.25,1)	0.034156964
37	5	=BINOMDIST(5,37,0.25,1)	0.071139152
38	5	=BINOMDIST(5,38,0.25,1)	0.060448988
39	5	=BINOMDIST(5,39,0.25,1)	0.051216574
40	5	=BINOMDIST(5,40,0.25,1)	0.043273983
41	5	=BINOMDIST(5,41,0.25,1)	0.036466047
42	5	=BINOMDIST(5,42,0.25,1)	0.030650935
43	5	=BINOMDIST(5,43,0.25,1)	0.025700232
44	5	=BINOMDIST(5,44,0.25,1)	0.021498648
45	5	=BINOMDIST(5,45,0.25,1)	0.017943462
46	5	=BINOMDIST(5,46,0.25,1)	0.014943774
47	5	=BINOMDIST(5,47,0.25,1)	0.012419646
48	5	=BINOMDIST(5,48,0.25,1)	0.010301181
49	5	=BINOMDIST(5,49,0.25,1)	0.008527583
50	5	=BINOMDIST(5,50,0.25,1)	0.007046225
51	5	=BINOMDIST(5,51,0.25,1)	0.005811761
52	5	=BINOMDIST(5,52,0.25,1)	0.004785276

Parameters

	Version	Type	Increment	Option	Derived	Unit	Data Type
Outcome IMPC_VIA_001_001	1.1	Simple Parameter		Homozygous - Viable Homozygous - Lethal Homozygous - Subviable			TEXT
Additional Outcome IMPC_VIA_002_001	1.1	Simple Parameter		Homozygous - Reduced Life Span Homozygous - Sick Mouse			TEXT
Total pups IMPC_VIA_003_001	1.1	Simple Parameter				count	INT
Total pups WT IMPC_VIA_004_001	1.1	Simple Parameter				count	INT
Total pups heterozygous IMPC_VIA_005_001	1.0	Simple Parameter				count	INT
Total pups homozygous IMPC_VIA_006_001	1.0	Simple Parameter				count	INT
Total male WT IMPC_VIA_007_001	1.0	Simple Parameter				count	INT
Total male heterozygous IMPC_VIA_008_001	1.0	Simple Parameter				count	INT
Total male homozygous IMPC_VIA_009_001	1.1	Simple Parameter				count	INT
Total male pups IMPC_VIA_010_001	1.0	Simple Parameter				count	INT
Total female WT IMPC_VIA_011_001	1.0	Simple Parameter				count	INT
Total female heterozygous IMPC_VIA_012_001	1.0	Simple Parameter				count	INT
Total female	1.0	Simple				count	INT

	Version	Type	Increment	Option	Derived	Unit	Data Type
homozygous IMPC_VIA_013_001		Parameter					
Total female pups IMPC_VIA_014_001	1.1	Simple Parameter				count	INT
Free Comment IMPC_VIA_016_001	1.0	Simple Parameter					TEXT
Average litter size IMPC_VIA_017_001	1.0	Simple Parameter					FLOAT
P-value for outcome call IMPC_VIA_032_001	1.2	Simple Parameter			IMPC_VIA_006_001 IMPC_VIA_003_001 IMPC_VIA_031_001 get_binomial_distribution_p_value		FLOAT
% pups WT IMPC_VIA_015_001	1.2	Simple Parameter			IMPC_VIA_004_001 IMPC_VIA_003_001 /	%	INT
% pups heterozygous IMPC_VIA_018_001	1.2	Simple Parameter			IMPC_VIA_005_001 IMPC_VIA_003_001 /	%	FLOAT
% pups homozygous IMPC_VIA_019_001	1.1	Simple Parameter			IMPC_VIA_006_001 IMPC_VIA_003_001 /	%	FLOAT
% male WT IMPC_VIA_020_001	1.1	Simple Parameter			IMPC_VIA_007_001 IMPC_VIA_010_001 /	%	FLOAT
% male heterozygous IMPC_VIA_021_001	1.1	Simple Parameter			IMPC_VIA_008_001 IMPC_VIA_010_001 /	%	FLOAT
% male homozygous IMPC_VIA_022_001	1.1	Simple Parameter			IMPC_VIA_009_001 IMPC_VIA_010_001 /	%	FLOAT
% female WT IMPC_VIA_023_001	1.1	Simple Parameter			IMPC_VIA_011_001 IMPC_VIA_014_001 /	%	FLOAT
% female heterozygous IMPC_VIA_024_001	1.1	Simple Parameter			IMPC_VIA_012_001 IMPC_VIA_014_001 /	%	FLOAT
% female homozygous IMPC_VIA_025_001	1.1	Simple Parameter			IMPC_VIA_013_001 IMPC_VIA_014_001 /	%	FLOAT

Metadata

	Version	Type	Increment	Option	Derived	Unit	Data Type
Female age earliest start IMPC_VIA_026_001	1.1	Procedure Metadata				Weeks	INT
Female age oldest end IMPC_VIA_027_001	1.1	Procedure Metadata				Weeks	INT
Time of dark cycle start IMPC_VIA_028_001	1.1	Procedure Metadata					TIME
Time of dark cycle end IMPC_VIA_029_001	1.0	Procedure Metadata					TIME
Age of pups at genotype IMPC_VIA_030_001	1.1	Procedure Metadata				Weeks	INT
Breeding Strategy IMPC_VIA_031_001	1.0	Procedure Metadata		HetXHet			TEXT