Viability Primary Screen IMPC_VIA_001

Purpose

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

Experimental Design

- Monitor genotypes of Het X Het breeding units; score genotypes of at least 28 live pups, unless four or more hom pups are produced before this threshold is reached. (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 live pups when genotyped, unless four or more hom pups are produced before this threshold is reached.
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, unless four or more hom pups are produced before this threshold is reached, in which case a viable call is valid.

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 and Metadata

Total pups IMPC_VIA_003_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

WT Male Ratio IMPC_VIA_020_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_007_001', 'IMPC_VIA_010_001')

Heterozygous Female Ratio IMPC_VIA_024_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_012_001', 'IMPC_VIA_014_001')

P-value for outcome call IMPC_VIA_032_001 | v1.2

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

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Total pups homozygous IMPC_VIA_006_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Free Comment IMPC_VIA_016_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

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Total male pups IMPC_VIA_010_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Total female WT IMPC_VIA_011_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Viability Outcome IMPC_VIA_001_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** true

Options: Homozygous - Viable, Homozygous - Lethal, Homozygous - Subviable, Hemizygous - Lethal, Hemizygous - Viable,

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Total pups heterozygous IMPC_VIA_005_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

WT Pups Ratio IMPC_VIA_015_001 | v1.3

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_004_001', 'IMPC_VIA_003_001')

Total pups WT IMPC_VIA_004_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Heterozygous Pups Ratio IMPC_VIA_018_001 | v1.2

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_005_001', 'IMPC_VIA_003_001')

Time of dark cycle end IMPC_VIA_029_001 | v1.0

procedureMetadata

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

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Total female heterozygous IMPC_VIA_012_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Additional Outcome IMPC_VIA_002_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** true

Options: Homozygous - Reduced Life Span, Homozygous - Sick Mouse,

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Total female homozygous IMPC_VIA_013_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Female age oldest end IMPC_VIA_027_001 | v1.1

procedureMetadata

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Unit Measured: Weeks

Total female pups IMPC_VIA_014_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Homozygous Female Ratio IMPC_VIA_025_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_013_001', 'IMPC_VIA_014_001')

Age of pups at genotype IMPC_VIA_030_001 | v1.1

procedureMetadata

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: Weeks

Total male homozygous IMPC_VIA_009_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Additional Subviable Outcome IMPC_VIA_033_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Options: Hemizygous - Subviable, Heterozygous - Subviable,

Breeding Strategy IMPC_VIA_031_001 | v1.0

procedureMetadata

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Options: HetXHem, HetXWT, HetXHet, HomXHet, HetXHom,

Total male WT IMPC_VIA_007_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

WT Female Ratio IMPC_VIA_023_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_011_001', 'IMPC_VIA_014_001')

Heterozygous Male Ratio IMPC_VIA_021_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_008_001', 'IMPC_VIA_010_001')

Total male heterozygous IMPC_VIA_008_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false

Unit Measured: count

Female age earliest start IMPC_VIA_026_001 | v1.1

procedureMetadata

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Unit Measured: Weeks

Average litter size IMPC_VIA_017_001 | v1.0

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

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Homozygous Pups Ratio IMPC_VIA_019_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_006_001', 'IMPC_VIA_003_001')

Homozygous Male Ratio IMPC_VIA_022_001 | v1.1

simpleParameter

Req. Analysis: false **Req. Upload:** false **Is Annotated:** false

Derivation: div('IMPC_VIA_009_001', 'IMPC_VIA_010_001')

Time of dark cycle start IMPC_VIA_028_001 | v1.1

procedureMetadata

Req. Analysis: false **Req. Upload:** true **Is Annotated:** false