Acute myeloid leukemia is a complex hematological malignancy with high molecular heterogeneity. JAX offers AML patient-derived xenograft (PDX) models with varying mutational profiles and treatment histories. These models are available for analyzing the effectiveness of potential new drugs—alone or in combination—to treat AML. These PDX models (Townsend et al.) have been engrafted in the highly immunodeficient NSG™-SGM3 (stock #013062), the mouse strain that most effectively engrafts human myeloid leukemia.

Robust engraftment of the primary AML samples in NSG™-SGM3 mice has been confirmed. This multi-allelic strain combines an immunodeficient environment with the transgenic expression of three human cytokines (SCF, GM-CSF, & IL-3) supportive of human myeloid cell expansion.

Average time to confirm AML engraftment in the peripheral blood of NSG™-SGM3 mice is 8 weeks post injection.

Client sponsored efficacy studies can be executed by the JAX® In Vivo Pharmacology Service group.

Engrafted mice can be delivered to client site.
# MODEL SPECIFICATIONS

## SUMMARY OF AML MODEL SPECIFICATIONS

<table>
<thead>
<tr>
<th>Model Number</th>
<th>Diagnosis</th>
<th>Mutational Profile</th>
<th>NSG™-SGM3 Engraftment</th>
<th>Ara-C Responsive</th>
</tr>
</thead>
<tbody>
<tr>
<td>J000106132*</td>
<td>Acute Myelocytic Leukemia</td>
<td>FLT3+, NPM1+, DNMT3A+, and IDH1+</td>
<td>20% AML at 8 weeks</td>
<td>Yes</td>
</tr>
<tr>
<td>J000106134*</td>
<td>Acute Myelocytic Leukemia, M4</td>
<td>FLT3+ and NPM1+</td>
<td>45% AML at 8 weeks</td>
<td>Yes</td>
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<tr>
<td>J000106566*</td>
<td>Acute Myelocytic Leukemia</td>
<td>TP53+</td>
<td>35% AML at 8 weeks</td>
<td>Yes</td>
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<tr>
<td>J000106124*</td>
<td>Acute Myelocytic Leukemia, secondary</td>
<td>No mutations identified</td>
<td>80% AML at 8 weeks</td>
<td>Not characterized</td>
</tr>
<tr>
<td>J000106143*</td>
<td>Acute Myelocytic Leukemia</td>
<td>TP53+ and CUX1+</td>
<td>20% AML at 8 weeks</td>
<td>Not characterized</td>
</tr>
<tr>
<td>J000106565*</td>
<td>Acute Myelocytic Leukemia M4/M5</td>
<td>FLT3 ITD+, FLT3 TKD+, and NPM1+</td>
<td>15% AML at 8 weeks</td>
<td>Not characterized</td>
</tr>
<tr>
<td>J000106569*</td>
<td>Acute Myelocytic Leukemia</td>
<td>FLT3-ITD+, and NPM1+</td>
<td>10% AML at 8 weeks</td>
<td>Not characterized</td>
</tr>
</tbody>
</table>

*Passaged Models

**J000106132**, **POSITIVE FOR FLT3, NMP1, DNMT3A, IDH1**

### Clinical History
- **Age:** 44
- **Sex:** Female
- **Treatment:** Allogeneic HSCT, Sorafenib, Hydroxyurea, Decitabine

### Diagnosis
- Acute Myelocytic Leukemia

### Karyotype
- Normal

### Mutational Profile
- FLT3+, NPM1+, DNMT3A+, IDH1+

### Engraftment in NSG™-SGM3 Mice
- ~20% AML at 8 weeks

### ARA-C RESPONSE IN AML MODEL J000106132

*Figure 3. PDX J000106132 averages 20% engraftment at 6 weeks and 70% at 8 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.*

*Figure 4. J000106132 AML NSG™-SGM3 mice. Growth rate of AML samples detected in peripheral blood in the presence or absence of Ara-C. Mice were engrafted with human AML cells (hCD33+) and treated +/- Ara-C (30mg/kg) for five consecutive days.*
**J000106134**, Positive for FLT3, NPM1

**Clinical History**
- Age: 58
- Sex: Male
- No treatment reported

**Diagnosis**
- Acute Myelocytic Leukemia, M4

**Karyotype**
- 46, XY

**Mutational Profile**
- FLT3+, NPM1+

**Engraftment in NSG™-SGM3 Mice**
- ~45% AML at 8 weeks

---

**ARA-C RESPONSE IN AML MODEL J000106134**

<table>
<thead>
<tr>
<th>Days Post Treatment</th>
<th>Control</th>
<th>Ara-C (10mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>30</td>
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<tr>
<td>21</td>
<td>20</td>
<td>20</td>
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</tbody>
</table>

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**J000106566**, Positive for TP53

**Clinical History**
- Age: 48
- Sex: Male
- No treatment reported

**Diagnosis**
- Acute Myelocytic Leukemia

**Karyotype**
- 44,X,-Y,del(5)(q13q35),-6,-7,-17, add(18)(p11.2),add(20)(q11.21q10), +der(?t(?;?11)?;q13?),+mar[cp11]/46,XY[9]

**Mutational Profile**
- TP53+

**Engraftment in NSG™-SGM3 Mice**
- ~35% AML at 8 weeks

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**ARA-C RESPONSE IN AML MODEL J000106566**

<table>
<thead>
<tr>
<th>Days Post Treatment</th>
<th>Control</th>
<th>Ara-C (30mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

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**PERCENT ENGRAFTMENT OF AML J000106134**

![Graph showing engraftment of AML J000106134 over weeks.]

**Figure 5.** PDX J000106134 averages 45% engraftment at 8 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.

**Figure 6.** J000106134 AML NSG™-SGM3 mice. Growth rate of AML samples detected in peripheral blood in the presence or absence of Ara-C. Mice were engrafted with human AML cells (hCD33+) and treated +/- Ara-C (30mg/kg) for five consecutive days.

**PERCENT ENGRAFTMENT OF AML J000106566**

![Graph showing engraftment of AML J000106566 over weeks.]

**Figure 7.** PDX J000106566 averages 10% engraftment at 6 weeks and 35% at 8 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.

**Figure 8.** J000106566 AML NSG™-SGM3 mice. Growth rate of AML samples detected in peripheral blood in the presence or absence of Ara-C. Mice were engrafted with human AML cells (hCD33+) and treated +/- Ara-C (30mg/kg) for five consecutive days.
J000106124*, NO MUTATIONS IDENTIFIED

**Clinical History**
- Age: 75
- Sex: Male
- No treatment reported

**Diagnosis**
- Acute Myelocytic Leukemia, secondary

**Karyotype**
- 46, XY, +11

**Mutational Profile**
- No mutations identified

**Engraftment in NSG™-SGM3 Mice**
- ~80% AML at 8 weeks

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![Figure 11. PDX J000106124 averages 80% engraftment at 8 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.](image1)

J000106143*, POSITIVE FOR TP53, CUX1

**Clinical History**
- Age: 48
- Sex: Male
- Treatment: Induction 7+3 x 2, Salvage MEC

**Diagnosis**
- Acute Myelocytic Leukemia

**Karyotype**
- 44, X,-Y, del(5)(q13q35),-6,-7, -17, +add(18)(p11.2), +add(20)(q11.2), +i(21)(q10), +der(21)(q10;11)?, +mar[c11]/46,XY[9]

**Mutational Profile**
- TP53+, CUX1+

**Engraftment in NSG™-SGM3 Mice**
- ~20% AML at 8 weeks

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![Figure 12. PDX J000106143 averages 50% engraftment at 12 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.](image2)
J000106565*, POSITIVE FOR FLT3 ITD, FLT3 TKD, NPM1

**Clinical History**
- Age: 61
- Sex: Male
- Treatment: Induction chemotherapy, Consolidation HiDAC, Allogeneic HSCT

**Diagnosis**
- Acute Myelocytic Leukemia M4/M5

**Karyotype**
- 47,X,Y,del(6)(q15q21),+8,+14.del(15)(q12q15)
- [17]/47, idem; der(1)t(1;1)[p36.1q44][2]/47; idem, t(1;9)[q23;q34][1].

**Mutational Profile**
- FLT3 ITD+, FLT3 TKD+, NPM1+

**Engraftment in NSG™-SGM3 Mice**
- ~15% AML at 8 weeks

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Figure 13. PDX J000106565 averages 15% engraftment at 8 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.

J000106569*, POSITIVE FOR FLT3-ITD, NPM1

**Clinical History**
- Age: 55
- Sex: Male
- Treatment: Induction, Consolidation

**Diagnosis**
- Acute Myelocytic Leukemia

**Karyotype**
- 46, XY[cp20]

**Mutational Profile**
- FLT3-ITD+, NPM1+

**Engraftment in NSG™-SGM3 Mice**
- ~10% AML at 8 weeks

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Figure 14. PDX J000106569 averages 10% engraftment at 8 weeks and 57% at 12 weeks post engraftment in peripheral blood of NSG™-SGM3 mice.
FAQ

In which mouse models were engraftment levels tested?
The currently available models are confirmed to engraft in the NSG<sup>TM</sup>-SGM3 mice.

What engraftment levels do you typically see?
Greater than 5% AML in the peripheral blood of NSG<sup>TM</sup>-SGM3 mice 10-16 weeks post engraftment.

How many AML engrafted mice can be included per order or on study with JAX?
A minimum of 15 mice is required. Approximately 100-500 mice in total can be engrafted depending on the model of interest.

What are passaged AML models?
Some AML tumor models in our portfolio were passaged in vivo. This approach allows JAX to continuously supply the models and retain inventory for use in further studies at later dates if needed.

REFERENCES

Elizabeth C. Townsend, et al. The Public Repository of Xenografts Enables Discovery and Randomized Phase II-like Trials in Mice, Cancer Cell, Volume 29, Issue 4, 2016, Pages 574-586, ISSN 1535-6108
