Life Whisperer
AI Enhanced Fertility

Life Whisperer Genetics Clinical Summary

Why Life Whisperer Genetics works.

Life Whisperer uses the most cutting-edge machine learning and computer vision methodologies to analyze thousands of embryo images and assess the genetic integrity (ploidy status) of blastocyst stage embryos. An embryo that has the correct number of chromosomes is called a euploid embryo, whereas an embryo that does not have the correct number of chromosomes is called an aneuploid embryo. Embryo ploidy status is usually evaluated using invasive embryo biopsy followed by genetic testing; this procedure is called pre-implantation genetic testing for aneuploidies (PGT-A).

The Life Whisperer AI alternatively works by non-invasive analysis of embryo images to identify complex visible patterns that are unknown to humans. The AI gives a score for each embryo that reflects how likely the embryo is to be euploid, ranging from 0 (least likely to be euploid) to 10 (most likely to be euploid) – this is called the *euploid score*.

The AI was trained on a cleansed dataset of 5,050 images and their corresponding PGT-A outcomes, from 2,438 consecutively treated women from five different laboratories. This training set was drawn from a larger set of 14,675 images, using a sophisticated data cleansing methodology to remove mislabeled data (patent pending). The AI was then blind tested on an additional 5,977 images from 2,903 patients to evaluate its ability to *enrich* for euploid embryos by ranking embryos according to *euploid score* within an embryo cohort (~60:40 ratio of euploid to aneuploid embryos).

The test was performed using a cohort ranking study as follows:

- Embryo images in the blind test set were randomized into simulated cohorts that consisted of embryos from different patients where the PGT-A outcome for each embryo was known. Each simulated cohort represented a hypothetical embryo cohort from a single patient's IVF cycle.
- Cohorts were an average of 10 embryos each, based on cohort sizes drawn from a distribution of actual embryo cohort sizes obtained from a clinical dataset (excluding cohorts of a single embryo).
- Images in the blind test set were initially randomized into ~100 simulated cohorts, then re-randomized again approximately 1000 times to give a total of ~100,000 unique cohorts for analysis.
- The embryos in each simulated cohort were then ranked by Life Whisperer Genetics *euploid score* from highest to lowest.
- Cohorts with no euploid embryos were excluded when considering the top-ranked embryo. Cohorts with less than two euploid embryos were excluded when considering the top-two ranked embryos.

Scientific Results.

Using Life Whisperer Genetics, the probability of the top-ranked embryo being euploid in a given simulated cohort was **82.4%**.

The probability of at least one of the top-two ranked embryos being euploid was **96.3%**.

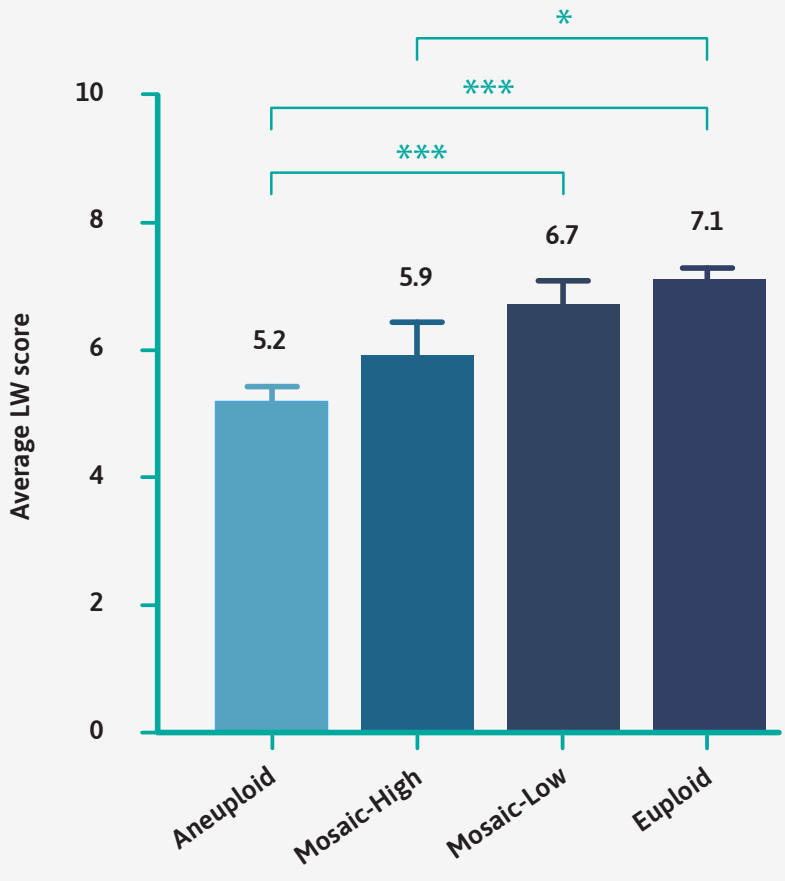
Finally, the probability of both top-two ranked embryos being euploid was **66.6%** - a **54.5%** improvement over random embryo selection.

The AI was also evaluated to determine correlation of the *euploid score* with the level of embryo euploidy or aneuploidy. Average scores were compared for full euploid and aneuploid embryos, and also for mosaic embryos consisting of a combination of normal (euploid) and abnormal (aneuploid) cells – **see Figure 1.**

As expected, full euploid embryos had a higher average *euploid score* (7.1/10) than full aneuploid embryos (5.2/10). Interestingly, mosaic-high embryos, with a higher proportion of aneuploid cells, had a lower average *euploid score* than mosaic-low embryos, with a lower proportion of aneuploid cells (5.9/10 and 6.7/10, respectively).

The average score for mosaic-high embryos was similar to that of aneuploid embryos, and was significantly lower than that of euploid embryos. Conversely, the average score for mosaic-low embryos was similar to that of euploid embryos, and was significantly higher than that of aneuploid embryos. These results show that the Life Whisperer Genetics *euploid score* may be used to differentiate embryos based on the level of mosaicism, which further supports the use of the AI for embryo ranking.

FIGURE 1



Average *euploid score* for full aneuploid and euploid embryos, and for mosaic embryos with either a high proportion of aneuploid cells (≥ 50%) or a low proportion of aneuploid cells (<50%).

Significant differences were evaluated using one-way ANOVA. Statistical significance is denoted by asterisks: * P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001.

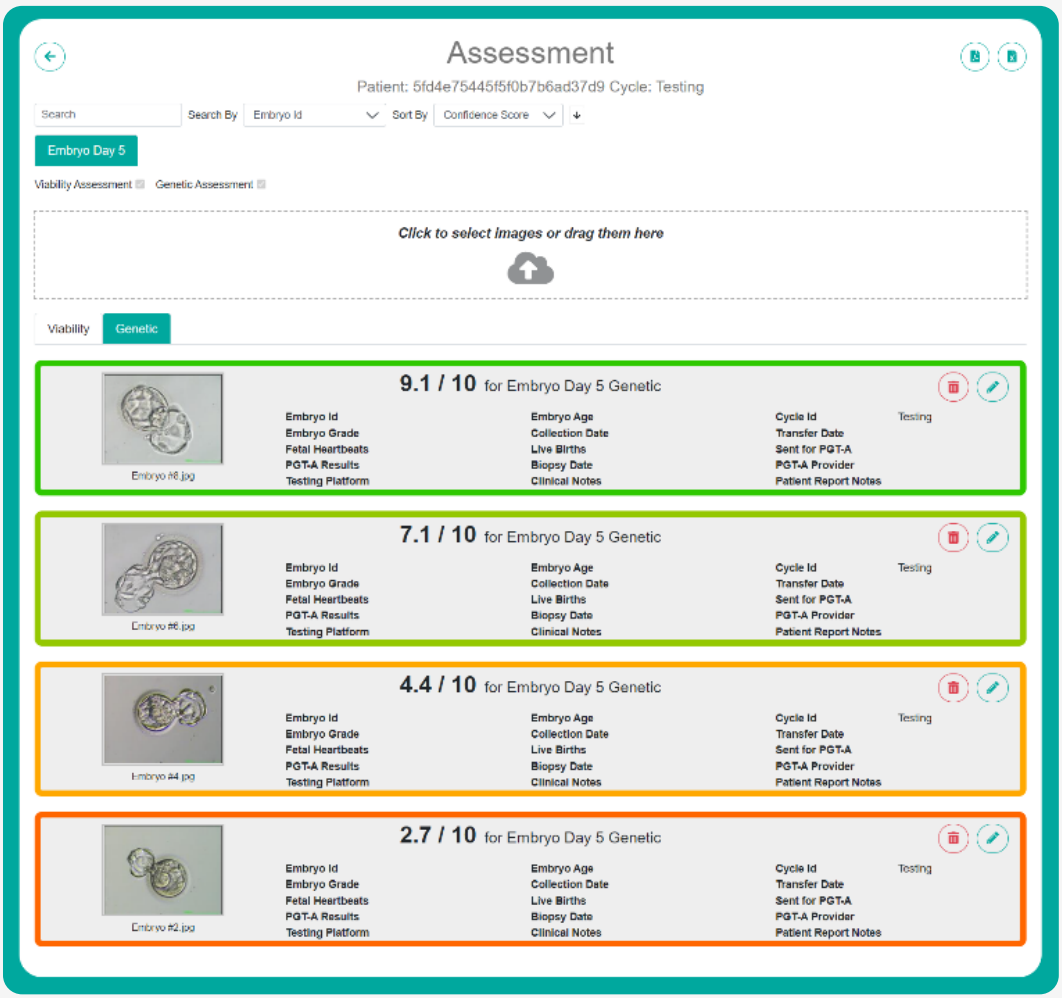
How do I use Life Whisperer Genetics in my clinic?

The Life Whisperer Genetics AI algorithm can identify complex features in the embryo that indicate whether it is euploid purely from the image alone, when uploaded to the Life Whisperer software application.

To use Life Whisperer Genetics, simply drag and drop images from the patient's embryo cohort onto the application interface. Results are provided in less than a minute, as shown in **Figure 2.**

Then simply select the top embryos in the cohort for euploid enrichment. The top-ranked embryo may be selected for transfer if desired, as being the most likely to be euploid (82.4% probability). Or, if confirmatory testing is desired, the top 2 (or more) embryos may be sent for additional PGT-A testing.

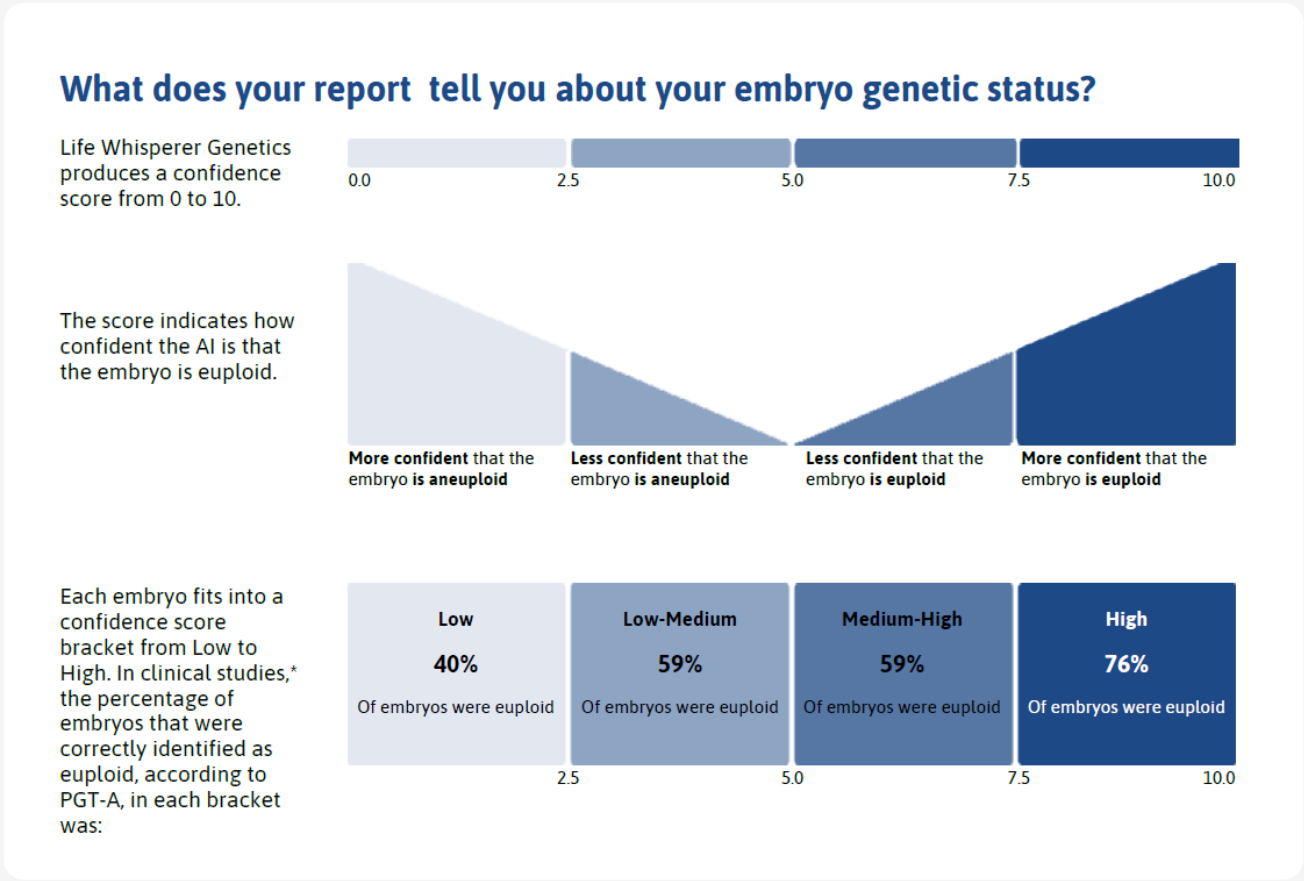
FIGURE 2



Example ranked embryo cohort by Life Whisperer Genetics, with *euploid score* displayed.

The downloadable Patient Report (available in the application) also provides the patient with information about the likelihood of their embryos being euploid – **see Figure 3**. This information shows that embryos of a high *euploid score* (7.5-10.0) are twice as likely to be euploid than embryos with a low *euploid score* (0.0-2.4), with an overall probability of 77% and 41%, respectively. The proportion of euploid embryos in the 2nd and 3rd quartiles were similar at 59%. This figure visually demonstrates the linear correlation of increasing *euploid score* with increasing percentage of euploid embryos (R^2 = 0.8911).

FIGURE 3



Patient Report excerpt showing correlation of Life Whisperer Genetics *euploid score* with rate of euploidy

Note that preliminary results also suggest that if an embryo has a high *euploid score* using the Life Whisperer Genetics application, as well as a high viability score using the Life Whisperer Viability application, there is an even greater likelihood of the embryo being euploid. Observations suggest Life Whisperer Genetics may be used for time-lapse images in clinical practice, however further validation of predictive accuracy is warranted.

For questions regarding the clinical summary, please email

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