Wound healing in 2D and 3D is critical constantly for many tissues in the body however, it’s known that aging and a number of diseases can decrease the body’s wound healing response. Collective cell migration is a necessary part of the wound healing process, and the nucleus is thought to be important in this mechanism. It’s found that with aging, genetic instability increases leading to a decrease in the stiffness of the cell nucleus and a compromise of chromatin architecture to where it is more condensed. So, we wanted to investigate how changes to chromatin and nuclear mechanics affects the cell migration process.

Based on this rationale we hypothesized that modifying nuclear mechanics and chromatin would influence 2D cell migration. To test this hypothesis, we used a model of the scratch wound assay with fibroblast cells as a standardized process to mimic wound healing at the skin. To do this, a layer of these cells was cultured, and a scratch was made to simulate a wound. Time lapse imaging was then used during the healing process to gather data on cell migration. Some groups during this process were treated with GSK126 to condense the chromatin architecture and others with Trichostatin A or TSA to decrease the nuclear stiffness.

When we applied the drugs here, this is what we saw for the control, GSK, and TSA groups over a 25 hour timeframe. Here we see that GSK and TSA both seem to have a decrease in wound healing when compared to the control group. Underneath you can see data for the 11 and 24 hour timepoints measuring what percentage of the wound was closed for each group. This data gives statistical significance that the drugs did in fact decrease migration.

We then wanted to get more information about how this decrease in migration is occurring so we repeated the experiment but tagged the cell nucleus in green as you can see here. From the zoomed in portions, you can see how the nuclear structure changes between groups and is clearly condensed for the GSK treatment. We then used an automated cell tracking software on these images visualized here with the paths of migrating cells marked with colored lines. We were then able to use this to create violin plots for cell specific migration parameters showing a box and whisker plot vertically as well as the data distribution along the sides. This data showed us that the TSA treatment decreased the speed and distance travelled of migrating cells and an even more drastic decrease in both was seen with the GSK treatment. Overall, this confirmed our hypothesis that altering nuclear mechanics and chromatin structure has an effect on cell migration and wound healing.

The future steps in this work include looking at the angular trajectory of migrating cells to see if there is an effect on the ability to follow migration gradients during this wound healing. Also, the development of a predictive biophysical model for determining migration parameters from chromatin and nuclear mechanic inputs. And the final step would be the adaptation of this study to include other cell types for further applied translational research.

I also don’t think the poster does much justice for the wound healing process we’re working with so if you’re interested, I have a couple time lapse videos here of what this really looks like.