# Comet Chip: A High-Throughput DNA Damage Sensor for Environmental Health Studies

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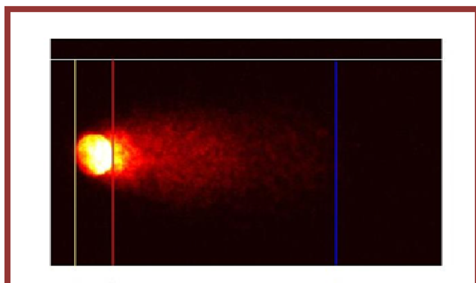
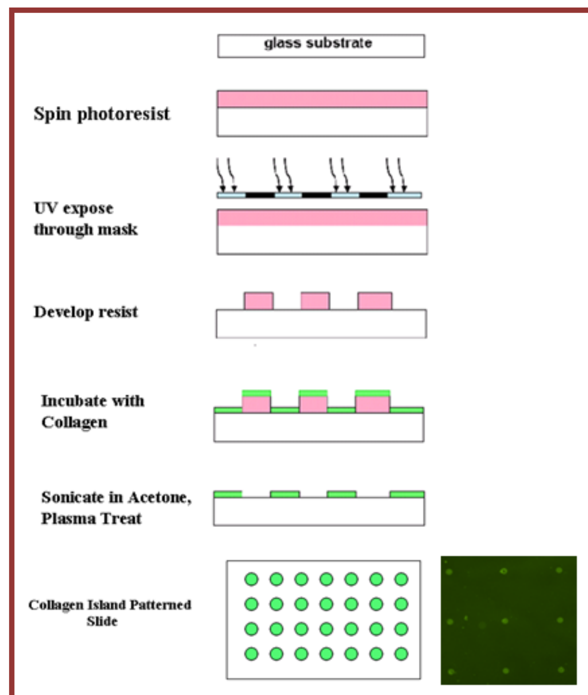
Environmentally and endogenously-induced DNA damage have long been known to contribute to cancer, aging, neurological disorders, and heritable diseases. Although effective methods for assessing DNA damage levels have been available for decades, and it is well established that information about DNA damage levels is highly useful both in the clinic and in population studies, measurements of DNA damage are far from routine. Technical difficulties associated with existing methods pose a major obstacle toward collecting data on DNA damage and repair in human samples. Our primary objective is therefore to develop faster, easier, and more robust methods to assess DNA damage and repair in human cells.

The core experimental method for this work is the single cell gel electrophoresis (SCGE) or 'Comet' assay. In this well-established assay, mammalian cells are embedded in agarose,



exposed to buffers that dissolve the cell membrane and denature the DNA, and subjected to electrophoresis. The principle of the comet assay is that damaged DNA (e.g., relaxed loops and fragments) migrates more readily than undamaged DNA, which tends to stay tightly wound within the nucleoid. The picture to the left shows an example of a damaged cell, and a clear 'tail' of damaged DNA is visible to the right of the nucleoid.

A major goal in this project is to develop patterning techniques to make it possible to analyze cells within a defined array. By arraying cells, we expect to reduce inter-cellular variability, which contributes to noise in this assay, and to increase experimental throughput by spatially encoding multiple experimental conditions on a single slide and processing them in parallel. We have explored a variety of approaches for arraying cells. In one approach, we used photo-patterning to create arrays of collagen islands. Cells were then allowed to attach to these islands and they were subsequently submerged into molten agarose and analyzed using standard comet analysis procedures. This approach proved to be effective for studying exposure-induced DNA damage, demonstrating that



arrayed adherent cells can be readily studied using the comet assay, thus facilitating studies of cells exposed to an array of conditions.

Currently, we are optimizing arraying methodology, quantifying assay sensitivity, and optimizing data collection and analysis. In the next phase of the project, we will create self-contained units that will serve to help standardize treatment conditions. Finally, we will collaborate with other research groups to apply this technology to study the levels of DNA damage in human cells from populations exposed to potentially genotoxic conditions. Ultimately, our goal is to provide assay conditions that are simple and easy enough to be useful in a broad range of studies of gene-environment interactions.