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August 2014

# Not Only in DNA's Hands

## Epigenetics has a large say in blood formation

Blood stem cells have the potential to turn into any type of blood cell, whether it be the oxygen-carrying red blood cells, or the many types of white blood cells of the immune system that help fight infection. How exactly is the fate of these stem cells regulated? Preliminary findings from research conducted by scientists from the Weizmann Institute and the Hebrew University are starting to reshape the conventional understanding of the way blood stem cell fate decisions are controlled thanks to a new technique for epigenetic analysis they have developed. Understanding epigenetic mechanisms (environmental influences other than genetics) of cell fate could lead to the deciphering of the molecular mechanisms of many diseases: immunological disorders, anemia, leukemia and many more. It also lends strong support to findings that environmental factors and lifestyle play a prominent role in shaping our destiny.

The process of differentiation – in which a stem cell becomes a specialized mature blood cell – is controlled by a cascade of events in which specific genes are turned "on" and "off" in a highly regulated and accurate order. The instructions for this process are contained within the DNA itself in short regulatory sequences. These regulatory regions are normally in a "closed" state masked by special proteins called histones to ensure against unwarranted activation. To access and "activate" the instructions, this DNA mask needs to be "opened" by epigenetic modifications of the histones so it can be read by the necessary machinery.

In a paper published in *Science*, Dr. Ido Amit and David Lara-Astiaso of the Weizmann Institute's Immunology Department, together with Prof. Nir Friedman and Assaf Weiner of the Hebrew University of Jerusalem, charted for the first time histone dynamics during blood development. Thanks to the new technique for epigenetic profiling they developed, in which just a handful of cells – as few as 500 – can be sampled and analyzed accurately, they have identified the exact DNA sequences, as well as the various regulatory proteins, that are involved in regulating the process of blood stem cell fate.

Their research has also yielded unexpected results: As many as 50% of these regulatory sequences are established and opened during intermediate stages of cell development. This means that epigenetics is active at stages in which it had been thought that cell destiny was already set. "This changes our whole understanding of the process of blood stem cell fate decisions," says Lara-Astiaso, "suggesting that the process is more dynamic and flexible than previously thought."

Although this research was conducted on mouse blood stem cells, the scientists believe that the mechanism may hold true for other types of cells. "This research creates a lot of excitement in the field, as it sets the groundwork to study these regulatory elements in humans," says Weiner. Discovering the exact regulatory DNA sequence controlling stem cell fate as well as understanding its mechanism hold promise for the future development of diagnostic tools, personalized medicine, potential therapeutic and nutritional interventions, and perhaps even regenerative medicine, in which committed cells could be reprogrammed to their full stem cell potential. ❚

*Dr. Ido Amit's research is supported by the M.D. Moross Institute for Cancer Research; the J&R Center for Scientific Research; the Jeanne and Joseph Nissim Foundation for Life Sciences Research; the Abramson Family Center for Young Scientists; the Wolfson Family Charitable Trust; the Abisch Frenkel Foundation for the Promotion of Life Sciences; the Leona M. and Harry B. Helmsley Charitable Trust; Sam Revusky, Canada; the Florence Blau, Morris Blau and Rose Peterson Fund; the estate of Ernst and Anni Deutsch; the estate of Irwin Mandel; and the estate of David Levinson. Dr. Amit is the incumbent of the Alan and Laraine Fischer Career Development Chair.*

# All-You-Can-Eat at the End of the Universe

At the ends of the Universe there are black holes with masses equaling billions of our sun. These giant bodies – quasars – feed on interstellar gas, swallowing large quantities of it non-stop. Thus they reveal their existence: The light that is emitted by the gas as it is sucked in and crushed by the black hole's gravity travels for eons across the Universe until it reaches our telescopes. Looking at the edges of the Universe is therefore looking into the past. These far-off, ancient quasars appear to us in their "baby photos" taken less than a billion years after the Big Bang: monstrous infants in a young Universe.

Normally, a black hole forms when a massive star, weighing tens of solar masses, explodes after its nuclear fuel is spent. Without the nuclear furnace at its core pushing against gravity, the star collapses: Much of the material is flung outwards in a great supernova blast, while the rest falls inward, forming a black hole of only about 10 solar masses.

Since these ancient quasars were first discovered, scientists have wondered what process could lead a small black hole to gorge and fatten to such an extent, so soon after the Big Bang.

In fact, several processes tend to limit how fast a black hole can grow. For example, the gas normally does not fall directly into the black hole, but gets sidetracked into a slowly spiraling flow, trickling in drop by drop. When the gas is finally swallowed by the black hole, the light it emits pushes out against the gas. That light counterbalances gravity, and it slows the flow that feeds the black hole.

So how, indeed, did these ancient quasars grow? Prof. Tal Alexander, Head of the Particle Physics and Astrophysics Department, proposes a solution in a paper written together with Prof. Priyamvada Natarajan of Yale University, which recently appeared in *Science*.

Their model begins with the formation of a small black hole in the very early Universe. At that time, cosmologists believe, gas streams were cold, dense and contained much larger amounts of material than the thin gas streams we see in today's cosmos. The hungry, newborn black hole moved around, changing direction all the time as it was knocked about by other baby stars in its vicinity. By quickly zigzagging, the black hole continually swept up more and more of the gas into its orbit, pulling the gas directly into it so fast, the gas could not settle into a slow, spiraling motion. The bigger the black hole got, the faster it ate; this growth rate, explains Alexander, rises faster than exponentially. After around 10 million years – a blink of an eye in cosmic time – the black hole would have filled out to around 10,000 solar masses. From then, the colossal growth rate would have slowed to a somewhat more leisurely pace, but the black hole's future path would already be set – leading it to eventually weigh in at a billion solar masses or more. ▮

*Prof. Tal Alexander's research is supported by the European Research Council.*

# Nanocubes Get in a Twist

Nanocubes are anything but child's play. Weizmann Institute scientists have used them to create surprisingly yarn-like strands: They showed that given the right conditions, cube-shaped nanoparticles are able to align into winding helical structures. Their results, which reveal how nanomaterials can self-assemble into unexpectedly beautiful and complex structures, were recently published in *Science*.

Dr. Rafal Klajn and postdoctoral fellow Dr. Gurvinder Singh of the Institute's Organic Chemistry Department used nanocubes of an iron oxide material called magnetite. As the name implies, this material is naturally magnetic: It is found all over the place, including inside bacteria that use it to sense the Earth's magnetic field.

Magnetism is just one of the forces acting on the nanoparticles. Together with the research group of Prof. Petr Král of the University of Illinois, Chicago, Klajn and Singh developed theoretical models to understand how the various forces could push and pull the tiny bits of magnetite into different formations. "Different types of forces compel the nanoparticles to align in different ways," says Klajn. "These can compete with one another; so the idea is to find the balance of competing forces that can induce the self-assembly of the particles into novel materials." The models suggested that the shape of the nanoparticles is important – only cubes would provide a proper balance of forces required for pulling together into helical formations.

The researchers found that the two main competing forces are magnetism and the van der Waals force. Magnetism causes the magnetic particles to both attract and repel one another, prompting the cubic particles to align at their corners. Van der Waals forces, on the other hand, pull the sides of the cubes closer together, coaxing them to line up in a row. When these forces act together on the tiny cubes, the result is the step-like alignment that produces helical structures.

In their experiments, the scientists exposed relatively high concentrations of magnetite nanocubes placed in a solution to a magnetic field. The long, rope-like helical chains they obtained after the solution was evaporated were surprisingly uniform. They repeated the experiment with nanoparticles of other shapes but, as predicted, only cubes had just the right physical shape to align in a helix. Klajn and Singh also found that they could get chiral strands – all wound in the same direction – with very high particle concentrations in which a number of strands assembled closely together. Apparently the competing forces can "take into consideration" the most efficient way to pack the strands into the space.

Although the nanocube strands look nice enough to knit, Klajn says it is too soon to begin thinking of commercial applications. The immediate value of the work, he says, is that it has proven a fundamental principle of nanoscale self-assembly. "Although magnetite has been well-studied – also its nanoparticle form – for many decades, no one has observed these structures before," says Klajn. "Only once we understand how the various physical forces act on nanoparticles can we begin to apply the insights to such goals as the fabrication of previously unknown, self-assembled materials." ▮

*Dr. Rafal Klajn's research is supported by the Abramson Family Center for Young Scientists; the estate of Olga Klein Astrachan; and the European Research Council.*