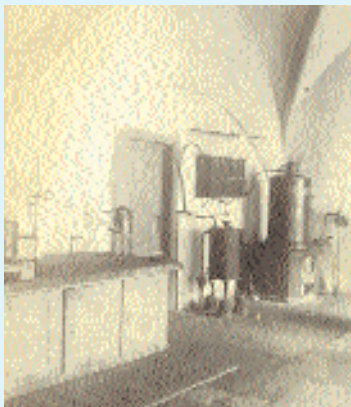


Rags before the riches: Friedrich Miescher and the discovery of DNA

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Like many success stories, the career of DNA as the molecule of heredity and icon of modern biology began under somewhat less glamorous circumstances. The story begins in 1844, one hundred years before Avery and his colleagues realised the significance of DNA as the genetic material (see accompanying article), with the birth in Basel of Friedrich Miescher, who went on to discover DNA at the age of 25.

Following a family tradition, Miescher trained as a doctor, but chose not to become a clinician — in part because of a hearing impairment. Instead, he went to Tübingen in 1868 and joined the lab of Felix Hoppe-Seyler, one of the pioneers of biochemistry, who had discovered hemoglobin just a few years before. At the time, the chemical characterisation of cellular contents was seen as a new and exciting possibility to understand the phenomena of cell growth and multiplication. The importance of these processes had been realised through microscopical observation, but what drove them or how they



DNA's 'cradle': The former kitchen of the castle in Tübingen was one of the first biochemistry labs in the world. Here Miescher discovered the 'nuclein'. (Picture: Fundus Tübinger Wissenschaftsgeschichte.)

were controlled was totally enigmatic.

As his pet cell for investigation, Miescher chose white blood cells, because they occurred as individual cells and were easy to obtain. Discarded bandages from a nearby surgical clinic provided pus from which intact white blood cells could be harvested. When Miescher exposed the cells to various salt solutions, they burst and a slimy porridge emerged that refused further analysis. As white blood cells were known to contain large nuclei, Miescher devised a method to further purify the cells and eventually obtain their nuclei. When he then subjected the nuclei to the same alkaline solutions as before, he noticed a precipitate that differed from previously characterised proteinaceous compounds in several ways. The precipitate was insoluble in the solutions proteins could normally be dissolved in; in contrast to proteins, the substance was rich in phosphorus; and, most notably, it was resistant to protein-digesting enzymes. Miescher concluded that he had discovered a new class of cellular substance, different from proteins, which he named, given its provenance, 'nuclein'.

Of course, Miescher could not have known what he had just discovered and unassumingly entitled the publication of his work, which was repeated by his fastidious supervisor: "On the chemical composition of the pus cells". The slimy precipitate from the nuclei of burst pus cells turned out later to be the molecule of heredity itself, DNA — something that can nowadays easily be isolated by biology undergraduates using similar chemical procedures as Miescher had used.

After a second post-doc studying neural circuits in the spinal cord, Miescher returned to



DNA's 'midwife': Friedrich Miescher (1844–1895) isolated DNA as a slimy substance from the nuclei of pus cells. (Picture: University of Basel.)

his home town of Basel and published another paper on nuclein in which he showed that it occurs in the spermatozoa of a wide range of animals. This connection between nuclein and the spermatozoa, which were known to be crucial for fertilisation, was the closest Miescher got to asserting the function of DNA. Indeed, he states: "if ... a specific substance is the cause of fertilisation, one would without doubt have to think of the nuclein."

Because of the poor working conditions in Basel, Miescher gave up on the nuclein and studied salmon in the nearby Rhine, as well as reviewing nutrition in Swiss prisons for the government. Unfortunately, Miescher did not live to see the consequences of his discovery. However, as Ralf Dahm, author of several articles on Miescher, states: "Miescher had an instinct for the key questions of his time and his scientific foresight was remarkable. Many of his theories on sexual reproduction and heredity proved to be correct." (For more on Miescher, see Ralf Dahm's article 'The molecule from the castle kitchen', Max Planck Research, 2004, Issue 2, 50–55).

Miescher died in 1895, aged only 51. Forty-nine years were to pass before it would be realised that the slimy substance isolated from pus was what carried genetic information.