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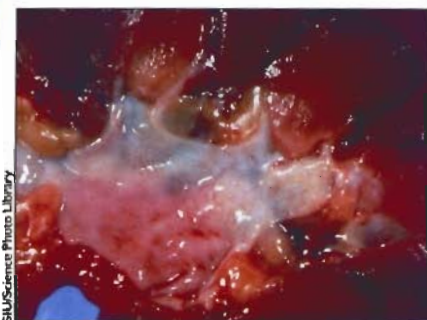
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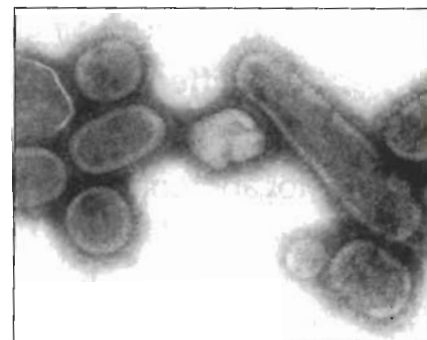
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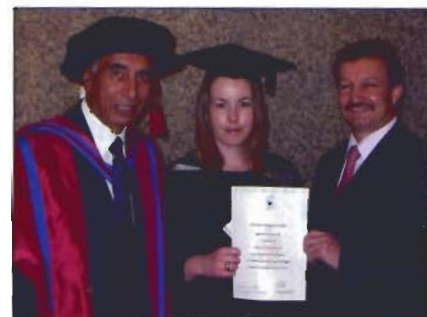
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Russian researchers Sergey V Malkov, Vladimir V Markelov, Boris I Barabanschikov and Maxim V Trushin and their Italian colleague Francesco Marotta believe that genome rejuvenation relies on the presence of silicon as an obligatory component of nucleic acids. Furthermore, they believe that enrichment of DNA with silicon can enhance normal regenerative events and perhaps inhibit cancer growth.

# Genome rejuvenation and its applications

Silicon is an abundant trace mineral in nature<sup>1</sup> and there is much published evidence to support its importance in both plants and animals.<sup>2-17</sup> Therefore, it would appear that silicon is not a biochemically inert element in plants and animals; indeed, an association with polysaccharides and wall-linked proteins has been demonstrated.<sup>18</sup> In rice, silicon is incorporated into links between lignin and carbohydrate,<sup>19,20</sup> and it has been demonstrated that silicon is connected with proteins (silicateins) in the sponge *Tethya aurantia*.<sup>21</sup> In 1993, silicon-responsive clones of complementary DNA (cDNA) were isolated from messenger RNAs (mRNAs).<sup>22</sup>

In animals, silicon is associated with various glycoproteins found, for example, in cartilage.<sup>23</sup> Other workers have demonstrated its importance in human bone and connective tissue formation,<sup>24</sup> as well as providing evidence for its role in the prevention of osteoporosis,<sup>25</sup> atherosclerosis<sup>26</sup> and some neurological disorders;<sup>27</sup> however, a connection with DNA has never been investigated.

To date, an indication that silicon compounds stimulate DNA synthesis in osteoblast-like cells<sup>28</sup> is the only report on its role in DNA activity. Nonetheless, evidence for the presence of silicon in the DNA molecule was presented as far back as 1975.<sup>29</sup> However, these results have yet to be reproduced or confirmed.

## Genome rejuvenation: an hypothesis

In 1989, a hypothesis for genome rejuvenation was suggested by scientists in the genetics department of Kazan State University in Russia.<sup>29</sup> The essence of the hypothesis is that DNA silicification takes place during transition from the senile form

‘There is evidence that silicon has a role in the prevention of osteoporosis, atherosclerosis and some neurological disorders’

to the juvenile form of nucleic acid, and was thought to be specific to *Bacillus subtilis* and other bacteria. Early studies showed that germanium and gallium (specific inhibitors of silicon and aluminium, respectively) influence the frequency of genetic transformation and competence.<sup>30,32</sup> These experiments confirmed the importance of silicon and aluminium during genetic transformation in soil bacilli. Aluminium was thought to act as an inhibitor of transcription at the DNA rejuvenation site.

Indirect evidence exists for the hypothesis. For example, Schroeder and co-workers investigated the role of various elements (lead, arsenic, germanium and gallium) on rat lifespan,<sup>33-35</sup> and only germanium resulted in a reduction. The effect of germanium could be due to its inhibition of silicon metabolism and a subsequent lack of silicon in DNA molecules.

Accumulation of iron and manganese in mouse DNA has also been observed, particularly in cells of the pancreas. High levels of iron and manganese have also been detected in silicophile plants during silicon starvation.<sup>31</sup> Thus, it is reasonable to suggest that accumulation of iron and manganese in mouse DNA is connected with alterations in silicon transport into DNA.

Weak suppression at the transcription level in *Drosophila melanogaster* (fruit fly) due to the action of antibiotics or inhibitors of transcription resulted in increased longevity. It is possible that inhibition of transcription resulted in reduced silicon loss from the fruit fly's chromosomes as well as delayed ageing.

The latter was also observed following addition of black silicon to the fly's food. This was supported by results of a study in which *B. oligonitrophilus* KU-1-treated barley was added to the fly's food (unpublished results).

In work on rats, a low-calorie diet during the early post-natal period resulted in a two-fold increase in lifespan; a phenomenon that



The importance of silicon has been studied in the fruit fly, *Drosophila melanogaster*.

can be explained by the maintenance of silicon levels (at least in the cells of the intestine), and an absence of the 'stress' associated with consumption of a high-calorie (fat) diet. Research in England has shown that addition of aluminium to a diet causes toxic effects, while addition of silicon reduces toxicity.<sup>14,15</sup> Furthermore, Carlisle and Curran<sup>36</sup> showed that silicon might prevent the formation of aluminium-associated lesions in the brain of rats.

Aluminium, a transcription blocker, is considered to be toxic in humans, animals and plants. In 1957, Williams and Vlamis<sup>37</sup> showed that the addition of silicon to plant growth solutions resulted in reduced manganese toxicity. Subsequently, numerous studies reported the protective effects of silicon in various plants, and possible mechanisms for these were suggested.<sup>38-41</sup>

### Applications to cancer treatment

The ability of *B. oligonitrophilus* KU-1 cells to increase normal intermutational (regenerative) events prompted the search for ways to increase such vitality in humans. Much initial work was performed by Tokin, a Russian embryologist, in the 1960s. He suggested that disruption of the various regenerative processes in the skin, breast and uterus, for example, resulted in the development of cancer. Of course, tumour development is more common in the elderly, in whom regenerative processes are limited. Furthermore, the importance of regenerative processes is demonstrated by the fact that it is very difficult to induce cancer (using X-rays or carcinogenic chemicals) in creatures (eg caudate amphibians) in which regenerative features are prominent. According to Tokin, regeneration and malignant growth are antagonistic events.

In addition to increasing age, other factors that may promote a decrease in regenerative capability include X-rays, ionising radiation and various carcinogenic agents; however, many such agents are used in cancer therapy, yet they can be both carcinogenic and mutagenic. According to Tokin's theory, frequently used anticancer drugs and radiotherapy decrease regeneration rather than increase it. Hence, it is necessary to look for factors that increase regeneration and resist malignant growth.

In recent experimental work, *B. oligonitrophilus* KU-1 (a donor of biologically active silicon) given orally restricted cancer growth.<sup>42</sup> It is possible that the bioavailable silicon released by *B. oligonitrophilus* KU-1 is utilised by polyhydroxylase, an obligatory enzyme required in the formation of connective tissue. Thus, restriction of metastatic growth can be explained in terms of the development of connective tissue, and this agrees with Tokin's theory that stimulation of normal regenerative processes results in the inhibition of tumour growth.

Moreover, there is a correlation between Tokin's theory, the genome rejuvenation hypothesis and results obtained at the

## 'In experimental work, *Bacillus oligonitrophilus* KU-1, which is a donor of biologically active silicon, restricted cancer growth'

Institute of Experimental Medicine, Central University of Venezuela. Lechin and colleagues showed that progressive reduction of growth hormone (GH) secretion by the pituitary gland occurs with ageing.<sup>43</sup> However, GH is a significant stimulator of immune function, and these authors clearly demonstrated that a neuropharmacological therapy aimed particularly at GH stimulation resulted in macrophage activation and subsequent inhibition of a range of tumours, including prostate, stomach and breast tumours, and of non-Hodgkin's lymphoma.<sup>43,44</sup>

### Future of silicon

Biologically active silicon would appear to have a role in the vitality of humans, animals and plants. Furthermore, according to the genome rejuvenation hypothesis, enhanced silicon metabolism may activate regenerative processes in humans. Clearly, the next step involves further study of silicon incorporation in DNA molecules, as well randomised, double-blind trials of *B. oligonitrophilus* KU-1 and its efficacy in the treatment of cancer. ■

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