On biotechnology

The new President of India, Mr K. R. Narayanan authored an article in Current Science several years ago (1989, 58, 534–536). We reproduce below an extract:

'... there is a bright future for the application of biotechnology for the benefit of mankind. I am not drawing the picture of a biotechnological paradise, but when I contemplate the ultimate fruits of this new branch of science and technology, I recall the lines of the poet who sang of an imaginary land:

Where there is neither death nor age
And the poor have all the money
The wells are full of wine
New bread grows on trees
And roasted pigs run about,
Crying, 'Eat me, if you please.'

There is, however, no Garden of Eden without a snake in it. Biotechnology has also its adverse effects. We do not yet know the long-term consequences of playing with the genes of living organisms, cloning them, splitting them, indeed tampering with the still inscrutable balance of nature and the ultimate mysteries of life. All one can say is that one has got to be extremely cautious and think deeply over the chain of possible consequences to mankind and to the universal order while we delve into the secrets of life, tampering with the geometry and chemistry of nature for satisfying the hunger, the thirst and the insatiable greed of man. We also ought to ask if the final solution to the endlessly increasing wants of man is only more and yet more production and the incessant multiplication of goods, or if some checks and restraints ought not to be put on this ceaseless escalation of human population and the even greater augmentation of human needs and cravings. Perhaps this is too philosophical a question to be posed to geneticists and biotechnologists. But then are not geneticists like particle physicists playing in those extreme border regions of science that are nearest to philosophy and metaphysics? ...

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Biodiversity – Patents are against national interests

In our own interest, we must not sign any 'Patent Treaty' because we shall lose considerably. The flora and fauna of this vast country with all possible diversities, is among the richest; but on record, the representative descriptions are mostly based on 'road-side surveys'. We have also labelled disciplines dealing with anatomy and taxonomy as 'obsolete' during the 1970s. Due to a variety of reasons, modern biology, genetic engineering and DNA technology have taken over as new 'high tech' needs of the country, with the result that researches in plant and animal taxonomy have been squeezed out of almost all major universities in India. Honestly, we cannot list even ten qualified experienced plant and animal taxonomists in each state of this vast country who are still in touch with their original interests. Actually, instead of modernizing areas of systematics, we have openly condemned these branches. However thanks to 'Biodiversity awareness' we are now searching our own torn bags. So, practically, what we know in Indian biodiversity in 1997 is only marginally greater than what we knew in 1960s.

Remarkably, all representatives of Indian flora and fauna must be present in several laboratories/herbaria of other countries as there has been a bonafide prequisite of 'getting it identified, confirmed and isotype deposited' elsewhere. All new species, microbial cultures, living and dried specimens are being sent to a large number of laboratories and research centres in other countries from several decades. Then, there are multinational or international institutes in India and abroad who have 100 times more resources and might have collected or rather obtained almost all relevant germplasm.

Whatever be the law, we can never protect our 'wealth of biodiversity'. Practically, we already have huge debts!. Why get bound in any treaty? On the contrary, we should resolve that anything that grows in India, found in India, is Indian and we shall use it. Why compartmentalize this country on the basis of biological wealth?

I totally agree with Suman Sahai (*Curr. Sci.*, 1997, **72**, 696–697) that patents favour only the patent holder, not the common man. On one hand we have progressed in science saying it is for the uplift of common man. Now, we however, are intent on commercializing every bit of 'leaf and flesh'. Actually the entire concept is inhuman and against international brotherhood. Patent is only commerce; science, not the least!!

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Sandur schist belt as a potential gold field

Manikyamba *et al.* (*Curr. Sci.*, 1997, **72**, 515–518) report that the gold mineralization occurs over a wide region in the Sandur schist belt (SSB) than it was hitherto known, and one can appreciate it may have the potential to turn out to be a future gold field. I have some comments to offer regarding the nature of gold mineralization and on the authors' statements regarding ore grade, mineability, etc.

The authors state that most of the gold is invisible and refractory (pp. 515, 516 and 518). Besides particulate gold, most of the gold reported from various localities in SSB can be described as 'ultrafine' gold, which comprises (i) free gold grains smaller than 5 μm in diameter, (ii) gold under 5 μm and physically absorbed onto iron and manganese oxides, clay minerals, sulphides, silicates and suspended matter, and (iii) colloidal gold (Xueqiu *et al.*[1]). The term 'refractory' has too broad a meaning. According to Gasparrini[2], if the ore microcomposition is known and the correct extraction technique for that microcomposition is employed, no ore is refractory, and she emphasizes employing microanalytical studies, especially for precious metals, as they occur in their host rocks in very low quantities which are often difficult to detect by other methods of mineral identification.

Regional geochemical mapping/surveys by employing low detection limits (at ppb level) and using low threshold values, lead to delineation of regional gold anomalous areas. The authors state that (p. 518), 'gold concentration of more than 10 ppb level is considered to be an anomaly in China, Canada and Australia'. In Axi deposit, China (Xueqiu *et al.*[1]), a regional anomalous area of approximately 80 km^2 was delineated by a 2.5 ppb contour line. The detailed survey that followed in the area delineated by 10 ppb contour line led to discovery of gold-bearing veins but no mineable ore deposit was found. However, low-concentration anomalies at 5 ppb level caused by ultrafine gold were investigated in another part of the same region and this led to the discovery of a large gold deposit.

Based on the preliminary mineralogical and geochemical studies, it is premature to say that this belt (do they mean the entire belt covering an area of 900 km^2) may be transformed into an *open cast mining goldfield* within a short time (concluding sentence on p. 518), when no detailed exploration has been carried out to assess the ore grade and the reserves available, also studies on the treatment or technique required for this type of ore to obtain maximum (+90%) metal recovery besides cost of roasting and grinding this type of fine gold ore are to be made. They declare 0.6 gpt gold ore will cover the total cost of open cast mining and extraction and zones of 1.5 gpt would be economically viable. This is like the proverbial – putting the cart before the horse. To mine a low-grade gold ore deposit, the mineable reserves (estimates based on detailed exploration) have to be large and amenable for large-scale mining operations and ensuring a high metal recovery (+90%) to keep the operative costs low for achieving economic viability.

1. Xueqiu Wang, Xuejing Xie and Shengyong Ye, *J. Geochem. Explor.*, 1995, **55**, 93–101.
2. Gasparrini Claudia, *Gold and Other Precious Metals (From Ore to Market)*, Springer-Verlag, 1993, pp. 336.

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Response:

We thank K. R. Raghu Nandan for his interest in our study which aims to geochemically determine the possibility of finding workable gold deposits in the Sandur schist belt (SSB) of Karnataka. The following is our response to his comments.

1. Evidently the term refractory has been used in its broad sense wherein gold is not easily amenable to cyanidation. It is indeed well known, since long[1] that at the microscale level gold is present in different forms and presence of such submicron size gold is confirmed in our work by microprobe analysis (see p. 515). Invisible gold occurs either as submicroscopic inclusions within the host minerals, as solid solution or chemically bound gold, thus rendering gold refractory to conventional cyanidation.

2. One of the objects of the study is to quantitatively analyse some zones to ascertain, if their gold content can qualify for more detailed exploration, characterization and genetic studies. Such detailed follow ups are already in progress. If favourable depth parameter is established, possibly a few zones may turn out economically mineable. Thus a small beginning made at some suitable places may hopefully lead to an expanded activity.

3. As quoted by Raghu Nandan[2], when even 2.5 to 5 ppb levels have been carefully explored in other countries and sometimes with great success, then, it is a straightforward corollary that 10 ppb level would naturally imply an anomaly and deserves a closer follow up to check its economic feasibility. In this connection, it is relevant to note that Raghu Nandan[2] himself has observed that 'we have never adopted such an approach in our country'.

4. Our purpose in this study has been to apply a concept-based geochemical method for assessing potential of some new prospects/deposits, identification of which has eluded the nation for quite some time[3]. For this, the modern plate tectonic framework has been invoked to delineate and understand favourable conditions. This strategy has indeed allowed the recognition of certain broad zones of Au enrichment. However, as is the usual practice, these delineated regions require further scrutiny and much finer evaluation to narrow down the targets and estimate the feasibility.

5. We emphasize that, nowhere do we claim that entire SSB could be transformed to open cast mining. We re-stress that the quantitative investigations carried out so far have merely focused on the scientific and economic significance of SSB in light of the gold enrichment that took place in this belt due to plausible plate tectonic processes during late Archaean. The delineation of the potential zones, as reported here, clearly corroborated the validity of this approach and, consequently, it encourages one to adopt

similar strategy for quantitatively assessing other parts of the SSB and other similar schist belts of Indian Cratonic regions.

6. The criteria of 0.6 GPT and 1.5 GPT are the general rules of thumb, quite commonly applied for the evaluation of an industrial prospect. It is perhaps not impertinent to note in this context, that in this era of *virtual reality* the cart and horse rule is somewhat out dated. Current operational cost of open cast mining at Ajjanhalli (Chitradurga, Karnataka) is about Rs 50 PMT, and the metallurgical operational cost is about Rs 250 PMT. Hence, we have stated that mining and extraction cost is covered by 0.6 GPT gold. The zone of 1.5 GPT becomes an economically viable region and can absorb depreciation, interest and exploration expenses. It may be noted here that Telfer (Western Australia) economically treats 1.1 GPT gold dump leach with 0.3 GPT tail losses and Mt Leyshon (QLD) treats 1.4 GPT with 0.18 GPT tail losses (personal communication to R. H. Sawkar by David S. Tyrwhitt of Australia).

7. Since gold-containing sulphidic BIF's at several places are, thick and long enough there is indeed a strong possibility of open cast mining even at low concentrations. Further, abundant sulphidic BIF horizons are found in SSB and other belts of Dharwar Craton. Hence these horizons may have a large potential to eventually become sites of new mines

8. The findings reported were preliminary results of a two-year-old DST-sponsored project. The aim was to communicate the importance of the inferences drawn so far, which may encourage the researchers to more closely evaluate various suspect zones for viable gold deposits.

9. Preparation of bankable document, based on the detailed exploration programme and long-term feasibility of low-cost mining requires a large sum of money. This may be taken up by interested companies who may get prospecting leases. The message indeed to be conveyed in the paper is to project the fact that the invisible refractory low-grade gold prospects require different mode of exploration programmes than that adopted for visible high-gold content prospects.

10. The Government of India has liberalized its mining laws to attract investments and some mining companies believe that their odds of finding huge low-cost deposits are higher in these relatively unexplored terrains than in the picked over terrains of ancient workings in India. James U. Blanchard[4], editor of *Gold News*, says that new discoveries and rising prices could help some gold stocks double in the coming years. Unfortunately gold mining companies in India are not in the stock market because of our collective lethargy and the 'do nothing' attitude.

1. Burg, G. H., *Metall. U. Erz.*, 1930, **27**, 333–338.
2. Raghu Nandan, K. R., *J. Geol. Soc. India.*, 1996, **48**, 596–597.
3. Radhakrishna, B. P., *Mineral Resources of Karnataka*, Geological Society of India, Bangalore, 1996, pp. 471.
4. Blanchard, J. U., *Gold News Cover Story* – Despite Bre-X., companies are digging new mines around the world.

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A shot in the leg to treat blocked arteries

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Atherosclerotic disease of blood vessels in the leg is a common cause for suffering in the elderly. The arteries usually get narrowed due to fatty deposits and fibrous plaques. Occlusion of limb arteries and consequent reduction in blood flow to the limb can lead to disabling clinical symptoms such as pain at rest, ulcers in the skin and even suppuration of the toes. Smokers and patients with diabetes mellitus are more prone to severe affliction and in them, the disease tends to progress rapidly.

Medical treatment is ineffective when blood through the arteries is critically reduced. Operative treatment to re-establish blood flow consists of either opening up the artery and removing the offending atherosclerotic plaque (end arterectomy) or creating a bypass using venous or synthetic grafts. Currently, there are several other forms of treatment as well. The atherosclerotic plaque can be burnt off with laser or the obstructing lesion can be shaved off with a rotary cutting device. Narrowed arteries can also be dilated by introducing a balloon to the site of obstruction and suddenly inflating the balloon (balloon angioplasty). Arteries can be kept in the dilated state by inserting metallic or polymeric stents. These techniques are relatively safe and have acceptable success rates. However, in a significant number of patients, the arteries get occluded again. Moreover, the techniques are invasive and involve puncture of arteries at accessible sites and threading of catheters to the sites of lesion.

A novel approach to treatment of locally reduced blood supply is to induce controlled growth of new blood vessels in the region of ischaemia[1]. In recent years, considerable progress has been made in identifying and characterizing substances which regulate mechanisms of blood vessel formation (angiogenesis). In experimental animals as well as in patients, local application of angiogenic factors has been found to be promising to treat conditions with localized hypovascularity. Attempts are now being made to introduce or transfer genes encoding angiogenic factors to the arterial wall. Direct gene transfer to the arterial wall involves invasive techniques which are difficult to be performed in patients with extensive and diffuse vascular disease. Extensive calcification, which accompanies atherosclerosis also precludes gene transfer to smooth muscle cells in the arterial wall.

Jeffrey Isner's group at Tufts University School at Boston, has been in the forefront of angiogenic gene therapy for a number of years. They are engaged in identifying appropriate genes for targeting, developing suitable biological vectors for efficient gene transfer and also finding effective delivery techniques for gene therapy in peripheral vessel disease.

Isner and colleagues (Tsurami *et al.*), in a recent issue of *Circulation,* report a simple gene transfer approach for inducing angiogenesis[2]. They have demonstrated blood vessel growth in experimental animals, after injection of naked DNA encoding vascular endothelial growth factor (VEGF) into skeletal muscles in ischaemic limbs.

There have been previous reports on the feasibility and efficacy of direct intramuscular gene transfer of plasmid DNA with a variety of reporter genes[3]. The possibility of intramuscular gene transfer of naked DNA to achieve expression of angiogenic factors in the treatment of peripheral vascular disease is demonstrated for the first time.

Naked plasmid DNA encoding the 165 amino acid secreted form of human vascular endothelial growth factor (hVEGF-165) was injected at multiple sites into three major thigh muscles of hind limbs of New Zealand white rabbits. The limbs were earlier made ischaemic by excising the femoral arteries in the thighs. Thirty days after injection, increased number of capillaries, collateral blood vessel formation and improved blood flow and tissue perfusion could be demonstrated in the injected limb. VEGF mRNA was detected in the skeletal muscle from day 3 after transfection and evidence of gene expression at protein level was seen at 5 days after transfection.

Vascular endothelial growth factor was discovered by Senger and co-workers[4] in the early 1980s. At that time, it was identified as a vascular permeability factor (VPF) which increases leakage of cells, fluids and proteins across the vessel wall. Later, this heat stable 46 kD dimeric protein was found to have the ability to stimulate the growth of endothelial cells and promote angiogenesis[5]. The biological activities of VEGF are mediated by two transmembrane receptor tyrosine kinases, which are expressed on vascular endothelial cells and angioblasts, their embryonic precursors. During embryonic development these receptors play an important role in the development of blood vessels[6]. VEGF was cloned and characterized eight years ago.

Isner's group had shown earlier that VEGF can stimulate the development of collateral arteries in animal models of both peripheral and myocardial ischaemia[7,8]. They also demonstrated recently, that angiogenesis can be induced in patients by transferring ph VEGF gene directly to proximal regions of occluded arteries[9].

The demonstration of viability of intramuscular gene transfer of naked DNA to achieve local delivery of an angiogenic factor and the observation that transfection leads to angiogenesis and improved tissue perfusion are important for cardiovascular gene therapy in general. The technique may be employed for trans endocardial delivery of angiogenic factor in patients with coronary artery disease.

A disadvantage in using naked plasmid DNA is the low efficiency of gene transfer which results in low levels of gene expression. However, acute or chronic hypoxia associated with ischaemia has been shown to be a strong stimulus for upregulation of VEGF receptor gene expression and endothelial cells of ischaemic tissues are likely to be more responsive to VEGF[10]. Hypoxic skeletal muscle in comparison with normal muscle, has been shown to have increased uptake and expression of exogenous plasmid DNA[11]. Hence, Tsurumi *et al.*'s results are encouraging.

M. W. Majesky cautions that VEGF may cause leakage of vasoconstrictors and coagulation factors from vessels, resulting in constriction of arteries and clot formation, further reducing blood flow through ischaemic vascular bed[12]. He also draws attention to the potential for elevated levels of VEGF in blood to initiate latent tumour growth or exacerbate diabetic retinopathy.