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Editorial

Towards Self-sufficiency in Protein Hormones Production to Augment MOET Programme in India

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Editorial

Stanley Cohen and Herbert Boyer demonstrated the bacterial transformation by an externally added foreign DNA presented through an appropriate vector with a built in antibiotic resistance marker in early seventies of the 20th century. Thus began the story of Biotechnology not just as another branch of Biology with emphasis on applications but also the best bet among approaches to solve a range of societal problems like Infectious Diseases, Food and Nutrition security, population size increase and its effect on economic growth and prosperity etc. Biotechnology has justifiably raised the hopes of millions of humans in getting access to biopharmaceuticals based on the new recombinant DNA technologies. With an expanded definition, it also has registered spectacular progress in developing Stem Cell Technologies for therapeutic applications. Developing countries (read India and South Asian countries) face another peculiar problem in the Veterinary scenario. Notwithstanding the enormous size of farm animal population (e.g. goats, buffaloes, poultry etc.), per capita production of milk and other farm produce lags behind that of developed countries (read Europe and North America). A significant percentage of human population is below poverty line without access to nutritional security. Governments of the day thought that Multiple Ovulation and Embryo Transfer Technology (MOET) program should help in solving the problem by contributing to herd improvement. The water buffalo (*Bubalus bubalis*) was identified as the target animal for the Indian efforts. Recombinant pituitary hormones like Follicle Stimulating Hormone (FSH) but of homologous origin have to be produced in large scale to satisfy the demand for this hormone for successful implementation of this MOET program.

Our laboratory, set up in the University sector, both at Hyderabad and New Delhi, was interested In dissecting and hopefully understanding certain fundamental research problems in endocrinology like mechanism of hormone action, regulation of signal (i.e. Hormone) level in circulation etc. Our laboratory initiated, in late nineteen seventies, a long range research program in generating our own quality reagents like hormones and antibodies to enable and support such a research program on buffalo endocrinology. Over a period of a decade we were successful in producing on a large scale, physic-chemically and immuno-biologically characterized buffalo pituitary hormones like Luteinizing Hormone (LH), FSH, prolactin (PRL), Growth Hormone (GH), Thyroid Stimulating Hormone (TSH). Biochemical protocols were standardized to obtain homogeneous preparations of these proteinaceous hormones from buffalo pituitaries collected from abattoirs. We have reported that on average we obtain about 300mg, 4-5 mg, 3000mg, 5000mg and 3mg respectively of LH, FSH, PRL, GH and TSH per every kilogram of freshly frozen buffalo pituitaries. We characterized these pure preparations extensively for their physic-chemical, Immunochemical and biological characteristics. All the bioassays for the hormones were standardized to ascertain their bio potency. In addition, well characterized and specific polyclonal antibodies and a library of Monoclonal Antibodies (MAB) against these pituitaries were also generated. Sensitive Radioimmunoassays (RIAs) and ELISAs were standardized for measurement of circulatory hormones in buffaloes. During these studies we were fortunate to make some minor discoveries in basic endocrinology. Two of these deserve mention among others. Mention may be made of the finding that the oligosaccharides of buffalo LH were sulphated at sugar residues and of the discovery of presence of an unusual post-translational modification in buffalo and sheep PRL i.e. tyrosine-o-sulphate. The chemistry of the oligosaccharides of LH from cattle was found to be difficult to solve as the non-reducing end was resistant to both chemical and enzyme reactivity. This was the opinion of the existing lead scientists in USA at that time. We had a hunch that the sugar could have a small group blocking it. Learning from structures of glycosaminoglycan, we suspected that sulphate moiety could be the blocking group. Immediately we checked this by metabolic labeling experiments where pituitary derived cells were incubated with radioactive sulphate and looked for the label in the TCA precipatable and LH-antiserum precipatable radioactivity. We found. Hence we speculated that the oligosaccharide of buffalo LH was indeed sulphated. Within a span of three months two groups from USA and one group from India published results pointing to the same conclusion. When we extended such studies to understand the sulphate metabolism in buffalo and sheep pituitaries including transport, we observed that radioactivity was found in considerable quantity in a fraction called by others as 'discarded acid pellet' from which we had shown to be rich source of PRL. Further work showed that PRL was also sulphated but most of it was on the peptide back bone in the form of Tyrosine-O-sulphate. The physiological significance of micro heterogeneous forms of these protein hormones in general and presence of anti-angiogenic activity in lower size isoforms of buffalo PRL in particular was delineated later by further studies from our laboratory. A Korean girl Jaeok Lee who completed her PhD in our laboratory was responsible for the characterization of the anti-angiogenic property of PRL derived peptides.

The absence of progress in the government driven MOET program on buffaloes for various technical reasons and our own biochemical work on buffalo pituitary hormones crossed roads in

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late nineteen nineties due to a fortuitous meeting. It took another two decades before government started supporting our laboratory efforts in cloning and expressing the genes for these hormones. We collaborated with another laboratory in Bangalore in these efforts. The first report on these lines is coming out in the present issue of this journal. We have a long way to go in successfully cloning and expressing biologically active buffalo FSH, the most important of these hormones. Further we need to scale up the operations, get the product tested in live buffaloes before we can claim that we have contributed to our national governmental efforts to solve Nutrition security issue in our country [1]. This is a small step towards the goal of indigenous production of biopharmaceuticals by recombinant DNA techniques of our country.

Reference

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