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INDIGENOUS KNOWLEDGE, BIOINFORMATICS AND RURAL AGRICULTURE

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ABSTRACT

Advances in genomic sciences, together with a recognition of indigenous knowledge, as well as identification of socio-economic incentives that promote sustainable agriculture are three things that are essential for utilization and conservation of genetic resources.. Agricultural genomics is picking up momentum. The merging of biology and information technology has brought about the area of bioinformatics with powerful tools and applications. Local knowledge sources are important for optimal use of available resources and twenty first century agriculture. New partnerships in the social, computational and biological sciences are leading to a cross pollination of approaches to solve common problems. Current efforts are shared.

Key words: Genomics, Indigenous Knowledge, Bioinformatics, *C. elegans*, therapeutic, rural, Traditional medicine

INTRODUCTION

Genomics is a science that studies the whole genome (Collins et al 1998). Genomic science integrates traditional genetic disciplines with new technologies in molecular biology such as DNA analysis, bioinformatics and automated robotic systems. Complete genome sequences have been determined for over 180 organisms including the yeast *Saccharomyces cerevisiae*, the nematode *Caenorhabditis elegans*, the fruit fly

Drosophila melanogaster, the annual plant *arabidopsis*, the human, the chicken and bovine(Adams et al 2000, Lander et al 2001, Venter et al 2001)

New developments and technology in agriculture will play a key role in sustainable economic growth and food security globally (Frost and Sullivan 1999, Shane et la 2002). The sequencing of genomes relevant to agricultural production (such as the cow, chicken, *Campylobacter*, *Theileria parva* etc) and the resulting genomic technologies and bioinformatics resources will serve to increase the expertise in identifying economically important genes and traits in agricultural production. This will also promote conservation of genetic resources. Global collaborations in genomics have confirmed that most biologic functions are genetically conserved within and between species. This means that by studying related organisms, we acquire biologic knowledge that is broadly applicable. Such research directs much of current biology and is expected to yield new insight with potentials for management and utilization of resources. Further, commonalties between genomes of diverse organisms are allowing greater understanding to improve production, health and provision of therapeutics (O'Brien et al 1999, Matlakshmi 2001).

Overwhelming amounts of data are being collected stored and analyzed using highly efficient, fast and productive technologies of genomics. The primary genomic data types are DNA and protein sequences, genetic mapping data and data resulting from functional analysis. Much of the data are freely available to the public via the Internet and World-Wide-Web. High throughput screening strategies such as microarray analysis and data mining in silico provide novel approaches to analyzing biological systems in the context of whole genome sequences (Frost and Sullivan 1999, Gardner and Flores 1999).

The outputs of genomic research are changing our overall approach to solving biological problem in agriculture. Information technology support systems are used for the management of molecular, experimental, bibliographic and other biological and environmental data. These systems support data delivery and analysis for decision-making. There is increasing need to share data among researchers, policy makers, and the general public. More than ever before, the Internet, the World Wide Web, and digital library technology are helping to make data-sharing possible. This allows stakeholders to exchange experiences, methods, and best practices in data sharing. Agricultural databases

at centers and institutions around the nation and the world allow for continued data mining for improved food and fiber production (Wood 1999, Sugdent and Pensi 2000).

Knowledge Sources

Bioinformatics is a collective name used for computer approaches in fields such as molecular biology, biotechnology, medicine and agriculture. Broadly it includes the application of modern computers, telecommunications, networks, and databases, as well as more specialized tools such as Geographical information systems (GIS), image analysis, and statistical and modeling software. Both bioinformatics and GIS use digital maps, large databases, and research involving visualization, pattern recognition, and analysis. GIS techniques and tools are used to find and track large patterns, such as geographic distribution of diseases in human, animal, and plant populations. Bioinformatics generally looks at very small patterns, such as those in DNA structure that might predispose an organism to developing disease. Biological data includes nucleotide and amino acid sequences, protein structure data, protein-protein interaction data, protein-DNA interaction data, data on enzymatic and biochemical pathways, webs of neurological structures and pathways, population-scale data, large-scale gene expression data, ecological and environmental data, satellite data, large-scale weather and soil data among others. Thus bioinformatics provides information synthesis capabilities, large capacity computational systems and other infrastructure and tools for the documentation and analysis of accumulated data and knowledge (Sugden and Pensi 2000)

Indigenous knowledge (IK) is the systematic body of knowledge acquired by local people through the accumulation of experiences, informal experiments and an intimate understanding of the environment in a given culture (Warren and Cashmaer 1988, Warren 1992). Traditional knowledge refers to the knowledge, innovations and practices of local communities around the world. This knowledge acquired through experience accumulated over the centuries is adapted to the local culture and environment. Further, it is transmitted orally from generation to generation. The value and utility of this knowledge for rural development has gained recognition globally (<http://www.worldbank.org/afr/ik/default.html>, Eyzaguirre et al 2001). Databases and ways of integrating IK into computerized systems are being developed (Tabor and

Hutchinson 1994, Sugden and Pensi 2001). This knowledge is valuable to rural communities its custodians and to development of modern industry.

Rural agricultural development rests on the bedrock of IK. Agricultural practices, such as the development of plant species and animal breeds provide valuable genetic resources and products, such as foods, medicines and cosmetics. Any attempt to utilize the results of genomic science in agriculture stands to benefit from the integration of IK, the traditional knowledge and practice of local communities to utilize and conserve biodiversity and genetic resources (Lambert 2001). Functionally defined genes resulting from genetic research serve as raw material for improvements in health and production. Genomic sciences and the ability to manipulate the genetic codes of living things has set off an unprecedented industrial convergence: farmers, doctors and drug makers; companies, and information technologies - all are being drawn into the business of life science. For example rural development efforts such as the eco-tourism industry are expected to benefit from fitness and nutritional programs informed by increased understanding of the life sciences through genomics research.

Biotechnology can be defined as "any technique that utilizes living organisms (or parts of organisms) to make or modify products, to improve plants and animals or to develop micro-organisms for specific purposes." (Hobbelink, 1991). Thus, biotechnology is as old as mankind. Ancient farmers, women, and indigenous peoples, have been domesticating and cross-pollinating plants, cross-breeding and taming wild animals since the beginning of time. U.S. revenues from biotechnology increased from \$8 billion in 1992 to \$39.2 billion in 2003. (Ernst & Young 2004.)

Integration of Knowledge

The teaming up of bioinformatics, the myriad of genomics tools and studies available in the twenty first century with traditional and indigenous knowledge will serve to harness information that will not only help to address concerns regarding applications of biotechnology but will also be key to the identification of economic incentives that promote sound agricultural practices. Cross-pollination of databases of IK with bioinformatics and GIS may provide a stepping ground for the integration of knowledge sources and utilization of technologies of the genomics era and beyond to develop novel biotechnologies.

There have been successful efforts to cross-pollinate IK and Geographical information systems (Tabor and Hutchinson 1994, Trpathi and Bhattarya 2004) and bioinformatics (Campbell 2001). The combination of different types of information whereby the scientists' findings and the farmers' practical experience and knowledge are integrated would provide a more complete description of biodiversity and natural resources. This is important for sustainable agricultural production through collaborative learning of farmers and scientists sharing experiences and expertise. This will also lead to the validation and enrichment of both scientific and indigenous methods. Documentation of IK in computerized databases is important to dissemination sharing and use in similar situations. The available bioinformatics infrastructure and expertise would facilitate integration of knowledge. The challenge in building an indigenous knowledge base lies in understanding and reasoning with the aid of largely abstract, qualitative observations of the local environment.

What is at issue? Can a teaming up of such sources of knowledge help us address social issues such as the limits of human activity, social values, social relations and the distribution of decision-making power to impact agriculture and rural livelihoods in the twenty first century? Adoption and use of new genomic technologies have social consequences. This is exemplified by the intense public debate on ethical, economic, legal and emotional aspects of biotechnology and recognition of the need for funding for studies on the ethical legal and social implications of genomics studies (Collins et al 1998). As part of economic considerations to benefit agricultural productivity, prevent the expansion of farm land and help the preservation of biodiversity attempts to protect traditional, indigenous knowledge and preserve biodiversity through new international legislation are at embryonic states of development (Braus and Amman 2002). Increasing agricultural productivity is the most effective way to overcome the problem of insufficient food availability. Modern biotechnology is an important component in solving this problem. The significance of the social context of information has been recognized in genomic science. The ethical, legal and social implications (ELSI) of genomic studies and the role of folk perspectives and traditional knowledge especially for minority populations and people in areas of rural isolation have been established. (Collins 1998, Lander et al 2001, Braun and Ammann 2002). Social values include primary and

non-primary use values. The primary use values are based on the direct and future impact on final good production e.g. modified organisms, therapeutics or future benefits due to biodiversity. Non-use values are difficult to assess but accrue due to the sole existence of knowledge and biodiversity. Utilization of IK and the latest knowledge acquired through genomic sciences will influence decision-making to impact rural livelihoods.

ILLUSTRATIONS OF APPROACHES TO START THIS PROPOSED INTEGRATION

To tackle the demands of 21st century animal agriculture in particular health many resources and partners are needed (Delgado et al 2001). Disease susceptibility and refractiveness to treatment contributes to management problems in the livestock industry worldwide. Inflammatory and parasitic diseases are some of the costliest health problems to the livestock industry (Kahrs 2004). Local and indigenous communities have acquired a wealth of knowledge about the healing properties of plants, minerals, insects, microbes and animal parts which has been the basis of health and veterinary care (Swerdlow 2000). Research is needed to determine the effectiveness and toxicity of traditionally used herbs and other natural substances. This will help farmer's interest in alternative medicine and organic farming. Knowledge about the characteristics of a particular organism such as a plant and its properties as a healing substance gives medicinal organisms their social and economic value. Local communities would benefit from the convergence of indigenous knowledge and advances in the life sciences and bioinformatics to study understand and improve the food supply.

In order to contribute to the sustainability of rural agriculture studies are being conducted to

- a. Identify medicinal substance based on indigenous knowledge and using publicly available databases
- b. Critically evaluate these products using controlled functional genomics experiments and bioinformatics
- c. Increase awareness and asses perceptions about the technology used
- d. Disseminate outcomes

APPROACHES

a: Identification of medicinal substance from indigenous knowledge using publicly available databases:

Studies to evaluate the effectiveness of traditional therapeutics on inflammatory and parasitic process in livestock (cows and goats) and to establish models for comparative genomics analysis of functional consequences of exposure using cell and molecular biology, bioinformatics, and micro array analysis are ongoing. Neem (*Azadirachta indica*), wormwood (*Artemisia absinthium*), tobacco (*Nicotiana tabacum*) and garlic (*Allium sativum*) are examples of plants used in traditional medicine that are considered to possess anti-helminthic and anti-inflammatory properties (Swerdlow 2000). Diatomaceous Earth (DE), from deposits of diatomites fossilized sedimentary layers of diminutive phytoplankton called diatoms, is a natural insecticide promoted by farmers as an effective anthelmintic. Shitake mushrooms and milk whey both are considered immunomodulators. The main biologically active constituents of these selected agents are presented in Table 1.

Table 1: Selected medicinals and their biologically active constituents

Medicinal	Main Biologically Active Constituent
Garlic	Allicin
Tobacco	Nicotine Anabasine
Neem	limonoids,(eg azadirachtin, salannin, meliantriol, nimbin,, nimbidin
Wormwood	Thujone
Shitake	1-3 beta glucans and lentinan
Diatomaceous earth	Diatomites
Whey	Proteins

A search of the Entrez database of the NCBI was conducted to gather information on literature, genomic and chemistry data on selected immuno-modulators. (Table 2)

Table 2: Entrez database citings of selected traditional medicinals form the National center for biotechnology web site

Database	Traditional Medicine	Shitake Mushroom	Garlic	Tobacco	Wormwood	Whey	Diatomaceous Earth	Neem
PubMed	39308	2	2187	44770	447	2950	361	356
Books	2	1	142	1565		8	135	1
Pubmed Central	714	424	87	6816	13	461	51	8
OMIM		3		30		9	1	
Nucleotide	114	4200	778	56137	5	724	35	9
UniGene	229612	105		2		7		
Protein		811	472	6744	1	484		5
CDD	351			2		2		
Genome		10	7	56		2		
3D Domains	351	100	16	350		8	52	
Structure		17	3	66		7	9	
UniSTS		1		3		4		
Taxonomy			1	1				1
PopSet	1	21		22		2		5
Gene		31	41	536		91		
HomoloGene		29	4	66		21		
PubChemcompound		2	1	4	2	5	1	1
PubChemSubstance		4	4	12	6	12	2	8
GenomeProject	4	2	1	5		1	6	
Journals		1		3			19	
MeSH	2	1	2	58		12	2	
NLM Catalog	4185		44	1138	12	15		12

b: Controlled functional genomics experiments and bioinformatics

ANIMAL, PARASITE AND CELL STUDIES:

Plant and Diatome derived medicinals : A thorough assessment of the utility of medicinals Neem (*Azadirachta indica*), wormwood (*Artemisia absinthium*), tobacco (*Nicotiana tabacum*) and garlic (*Allium sativum*) plant extracts and Diatomaceous Earth (DE), from deposits of diatomites to control parasites and inflammation was conducted in goats. Packed cell volume

(PCV) and the FAMACHA eye color chart for anemia, body weight (BW), fecal eggs count (FEC), total white blood cells counts (TWBCC), and white blood cell differential counts (WBCDC) was compared in treated and untreated animals. Neem, tobacco, wormwood and DE showed promising immuno-modulating effect in infected goats. An organically approved Garlic extract did not reduce FEC or alleviate anemia at the concentrations tested. In summary the results of these controlled experiments showed that these traditional medicinals used by indigenous peoples were effective at modulating the immune response and indeed had efficacy in promoting health but were not effective in reducing worm burden or alleviating associated anemia. Molecular evaluation of effects using microarray analysis will be conducted

Gene Expression:

Mushroom Extracts: Phagocytic destruction of opsonized bacteria by bovine neutrophils (PMN) is mediated by receptors (FcR) binding IgM and IgG2. These receptors thus are essential components of the inflammatory response and associated apoptosis of PMN. Natural immunomodulators such as 1-3 beta glucans and lentinan have been identified in mushrooms. The objectives of this study were to evaluate aqueous extracts of shitake mushrooms for their effect on the modulation of immunoglobulin binding and Fc receptor expression on bovine PMN using flow cytometry. A differential effect was observed for the expression of bovine FcR genes essential to the destruction of pathogens

Bovine milk : Bovine milk whey has a long history of use in traditional medicine from the time of Hippocrates. It is also used in cancer AIDS and other conditions. Components of whey such alpha lactalbumin, beta-lactoglobulin, branched-chain amino acids, glycomacropeptides, immunoglobulins help in the fight against disease, promoting a healthy body.

Currently efforts are underway to use the E.coli K-12 microarray to assess the effects of bovine whey on gene expression in E.coli at the level of transcription. Two RNA isolation kits were evaluated. RNA quality and quantity was evaluated using gels, Optical Density readings and a Bioanalyzer. Using the RNeasy method exposure to whey samples appeared to adversely affect the quality and integrity of RNA isolated from E. coli. This may indicate a possible mode of action for immune components in bovine whey in combating E. coli infection in diseases such as mastitis.

FUNCTIONAL AND COMPARATIVE GENOMICS: The effects of traditional plant and animal derived therapeutics on animal health are being evaluated using functional and comparative genomics. By determining the function of components of the genome functional genomics is applied to pharmaceutical research and development. Comparative genomics is the analysis and comparison of genomes from different species, to gain a better understanding of how species have evolved and

Amplification of Eukaryotic mRNA: Bovine polymorphonuclear neutrophils are very important in the inflammatory response in conditions such as mastitis. In order to benefit from the recent sequencing of the bovine genome and the availability of commercial microarrays sufficient quantities of RNA are needed. It is possible to amplify the concentration of RNA from bovine neutrophils using newly available kits and procedures. This offers a viable approach for the evaluation of the therapeutic effect of traditional medicinals at the level of transcription on a genomic scale. Further the availability of primers and expressed sequence tags have been used for the identification of genes associated with inflammation using the polymerase chain reaction, sequencing and bioinformatics(Harris). This is very important to the generation of new therapeutics.

Model Organisms and screening systems

Model organisms offer a cost-effective way to follow the inheritance of genes (that are very similar to livestock genes or their pathogens) through many generations in a relatively short time. Comparative genomics conducts gene-based biology in model organisms (eg E.coli, yeast, worm and mouse) to identify and validate drug targets and to generate animal models for disease. Gene expression microarrays consisting of hundreds or even thousands of gene-specific DNA sequences bound to a solid matrix make it possible to analyze gene expression changes in a massively parallel fashion. Gene array data analysis programs employing clustering techniques have been developed to facilitate the identification of predictive "fingerprint" patterns of gene expression caused by exposure to various treatments. The power of this technology has already been demonstrated for drug screening applications. Analysis of several thousands of genes may reveal subsets of genes which provide predictive information. These subsets can be utilized for routine screening applications. Microarray gene expression profiling holds great promise for identifying drug effects and toxicity. It is a goal of this effort to validate the use of microarray

gene expression analysis in in vitro models for the purpose of screening, toxicology and safety testing of topically of traditional medicinals.

Both approaches are used to exploit *C. elegans* as a model organism to identify and characterize the functions of novel genes and their counterparts in parasitic nematodes and host species and investigate the mechanisms of action of pharmaceutical agents of relevance to agriculture. Other studies include the response of the *E.coli* genome to modulation by whey and functional genomics studies using bovine microarrays arrays. Publicly available computer programs are used to study multiple genomes and look for regions of similarity using tools such as BLAST from the National Center for Biotechnology Information.

Interdisciplinary collaboration and infrastructure:

A cross pollination of ideas and interdisciplinary collaboration are essential to the success of such an effort. A proposal to establish a center of excellence for studies in genomic diversity received internal funding. As part of an effort to increase capacity to conduct training in agricultural biotechnology and genomics a series of workshops were conducted on topics including the Field Guide to NCBI data bases, Vector NI suite, new gene discovery and microarray analysis. Such fora not only provided training but also promoted collaboration and networking across disciplines.

A comprehensive campus wide survey was conducted to plan for the establishment of a virtual center of excellence for studies in Genomic diversity and promote external and internal interdisciplinary collaboration. A website was established to promote collaboration and increase awareness (<http://www.ag.ncat.edu/academics/anisci/faculty/worku/index.htm>)

A bioinformatics learning facility and microarray core were established. The bioinformatics facility provides personal computers, software and access to the most powerful and up-to-date statistical and genetic analysis programs in collaboration with other bioinformatics centers in addition to publicly available databases and bioinformatics tools.

The DNA Microarray core uses technology that allows the simultaneous determination of the expression level of tens of thousands of genes and is equipped with supporting equipment for RNA isolation and analysis and PCR. Understanding the function of genes and other parts of the genome is known as functional genomics.

c. Collaborative efforts to assess perceptions about the technology used

Current collaborative efforts have commenced to use applied survey technology to assess perceptions and attitudes animal biotechnology in livestock in collaboration with the applied survey laboratory social scientist and to develop collaborative efforts in social values, GIS technology traditional medicine and farmers and community support. State-of-the-art survey methodologies, and computer and communications technologies allow for assessment of perceptions about technology and documentation from different knowledge sources. An understanding of perceptions of technologies and areas of community concern can be identified through collaborative scientific research investigations using applied survey methodology. The applied survey laboratory houses telephone survey stations, mail survey facilities and data entry/programming stations, computers and software for data analysis, graphics, word processing, communications, and computer-generated presentations. The laboratory is engaged in developing a repository of science based data to support applied research. The Group Systems® program offered by the laboratory allows for effective institution of extensive qualitative survey techniques. For example, participants are able to provide data in a manner in which confidentiality is very important. Therefore, the participants are willing to provide more complete and accurate data, especially to questions that are of a sensitive nature. (<http://www.groupsystems.com/company/index.htm>). The Option Finder ® program enables researchers the ability to conduct qualitative and quantitative research while traveling to different locations. This technology permits participants of the listening sessions to respond to questions by selecting the appropriate responses through the use of a special remote control device. These devices can also be utilized by the participants to rank responses in a particular order. Finally, reports can be generated at the conclusion of each listening session and copies of the report can be distributed to each of the participants (<http://www.optionfinder.com/optionfinder.html>). In addition the laboratory has the capability to utilize GIS to analyze data pertaining to the spatial characteristics of a study area. Primary survey data on health issues and biodiversity of an area can be linked with secondary GIS data on location, makeup of household, income level, education level, climate, and ethnicity. This will help explain behavior patterns in the context of current social, economic and the physical environment (<http://www.esri.com/>).

d. Disseminate outcomes: The outcomes of all research efforts are shared with stakeholders and contribute to the development of training initiatives. Long term plans are to ensure that research

and extension programs that build on the indigenous and traditional knowledge of farming communities contribute to local economies and enhance the environment. Through collaborations with the cooperative extension programs farmers impacted by the tobacco industry in North Carolina and small farmers are a target of focus. Several large projects in biotechnology like HUGO, the Human Genome project, have an “ELSI” component, dealing with ethical, legal and societal implications of biotechnology. This shows that some scientists realise that science cannot be seen as a human activity taking place in a void, without any connection to social and political realities. The issues involved in the interaction between biodiversity and biotechnology have far-reaching consequences and need to be subject to an open and knowledge-based dialogue in society. This dialogue should include different stakeholders, including farmers, diverse scientists, policy makers and communicators. Cultural values involved in farming and food production need to be taken into consideration, just as much as the emotional side of eating and drinking. A significant aspect of ethical behavior is openness. Transparent information is required both from scientists in non-commercial settings as well as from industry. Immediately divulging research results, by scientists personally to the interested public and to policy makers would help improve mutual confidence.

SUMMARY AND CONCLUSIONS:

Indigenous knowledge is being used in ethno botany and ethno veterinary medicine to identify and catalogue natural resources and their uses. Local resource managers possess a detailed understanding of resource values and management practices. Knowledge about the characteristics of a particular medicinal and its properties as a healing substance is what gives genetic resources (plants, animals, micro organisms) their social and economic value. This knowledge has been acquired through experience, trial and error and incremental refinement. A natural link to this knowledge is part of what fuels the curiosity of scientists trained with an awareness of this knowledge and exposure to traditional medicine. Scientific studies, documentation of knowledge and placing the information on public domains are important ways of validating IK and protecting ownership.

This work aims at the preservation and perpetuation of knowledge for the identification and conservation of genetic resources to ensure sustainability of agriculture through the utilization of the tools and infrastructure of genomic science. Studies have been initiated to identify and

systematically characterize medicinals used in traditional medicine for the purpose of controlling parasitic and inflammatory disease in livestock. The approach is based on the identification of these therapeutics from indigenous and traditional knowledge, using publicly available databases and peer-reviewed literature to supplement this information. Designing carefully controlled studies at the cellular, molecular and genomic levels to define and validate the value of these medicinals. These biological studies are coupled with an evaluation of the perceptions and social value of the technology and information acquired through collaboration with rural sociologists. Further this is shared through educational programs to farmers and other stakeholders. Thus, increased understanding and integration will translate to social benefits through creation of economic stimuli and collaborative utilization of resources. This will in turn translate to environmental incentives to protect natural environments. Benefit sharing encompasses collective ownership of knowledge innovation and utilization for the common good. Documentation of IK and public availability of controlled scientific studies incorporating the latest developments in genomic science can be accomplished through a teaming up of bioinformatics and indigenous knowledge through collaboration of farmers and scientist for the sustainability of agriculture.

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