Shortchanged:
Biotechnology and the Emerging Climate Market

a report prepared for
Californians for
GE-Free Agriculture

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Executive Summary

The failure of the first generation of agricultural biotechnology to deliver on its principal promises of higher yields and lower inputs set the industry on a defensive stance in the past decade. Unabated public rejection and key defeats, not least in California, has led to a thorough re-branding and re-packaging of the old transgenic manipulations. **The Biotechnology industry has found an emergent market for expansion driven by popular concern over Climate Change.**

"Climate Ready Crops" are more likely to be developed by non-transgenic methods. Traditional transgenic techniques do not lend themselves to develop crop varieties tolerant of abiotic stress. Meanwhile, public reluctance to embrace transgenic products does not abate. Both developments make non-transgenic methods such as Marker Assisted Selection (MAS) the primary likely avenue for the development of "Climate Ready Crops." Although MAS per-se is not a transgenic manipulation, it can be used rhetorically to mask the presence of transgenic constructs in parental lines and hybrids as they move through the long breeding pipeline.

The ecological effects of gene flow from crops produced for abiotic stress and transgenic biofuels will likely be greater than "first generation" transgenic crops. Gene flow from crops that are developed for extreme environments pose the threat of conferring this great phenotypic advantage to the recipients, including weedy relatives of the crop, which already are a problem as superweeds in the vicinity of current GM crops. Furthermore, manipulations of the cell-wall biochemistry proposed by biofuel-related initiatives is likely to lead to increased susceptibility of plants to pathogen/parasite attack. Conversely, proposed manipulations could spread to microbes and increase their capacity to break down plant cell walls and contribute to increases in pathogenicity.

Agroecological methods provide a better alternative than biotechnology in addressing challenges to agriculture that might arise from climate changes. Agricultural systems that are based upon diversification and lower inputs, that use already existing diversity and crop varieties and are under the stewardship and control of the producers and the public are locally adaptive and better suited to mitigate the negative effects that might arise from changing climates.

Transgenic plants may be more readily accepted as biofuels. Since biofuels are not ingested by humans there is likely to be less opposition from consumer groups and the public against the use of transgenic plants as biofuels as opposed to food or feed. Lower public scrutiny is compounded by a much lower degree of understanding of the novel crops involved in biofuels: trees, grasses, algae, microbes. We do not have the centuries of accumulated knowledge nor the scrutiny of modern science over those new crops before they are released into the environment.

Cellulosic and microalgal biofuels are unlikely to be commercially successful in the long run and are hyperbolic in their estimations of productivity and potential. The commercial viability of biofuels largely rests upon state subsidies and is impacted by fluctuating fossil fuel prices. This is not to undermine the point that serious questions remain about whether biofuels themselves represent any of the benefits they are supposed to bring. The biological viability of the current proposals of transgenesis in biofuels rides on manipulating processes that are very far from being understood, in organisms that we do not know how to manipulate as well as we do our crops. But transgenic products as part of the biofuel industry will likely increase in the future given current political trends.

Synthetic biology is genetic engineering by another name and is likely to fail. There are many reasons why synthetic biology should follow the unenviable steps of "first generation" transgenics, but a pragmatic look at market success shows that the "SynthBio" industry is actually on its way out, kept under "artificial respiration" by public support and subsidy. If first-generation transgenesis failed in its quest of control and reliability in dealing with relatively short inserts of DNA, there is no reason why a multiplication of transgenic manipulations with large numbers of inserts should be more predictable, controllable or reliable.

CA specialty crops will most likely not have transgenic varieties soon. While there is research involving transgenic modifications of specialty crops it is unlikely that there will be commercial development anytime soon as indicated by the stagnancy of field trials (Roundup Ready Onion might be an exception).

Transgenic safflower might see commercialization in the near future. Oils produced from transgenic plants are claimed to be free of DNA and therefore transgene free. For this reason transgenic safflower for oil might be commercialized soon. Absence of DNA is not neccesarily the case and the amount of DNA present in oils is contingent on the method of production.

Transgenic insects with gene drive systems must be opposed vigorously when and if they appear. Research is being done into linking transgenes to unstable genetic elements to control insect populations. This line of research and possible products should be opposed as they present a serious ecological threat.

Transgenic vaccines have largely remained underexposed to critical inquiry. They represent one of the most radical interventions, and paradoxically one of the most viable because of the simplicity of the viral systems as well as the political momentum in support of their development and release.

California plays a major role in the development of biotechnologies associated with Climate Change. Many of the research institutions and biotechnology corporations conducting research associated with Climate Change are located in California and especially in the San Francisco Bay Area. The plexus of public universities, federal institutions and private corporations, all bundled into an academic-military-industrial-corporate complex comprises a veritable "ecosystem of biotechnology" in California.

We suggest that the Cal GE-free coalition could well shift its focus from campaigning against the cultivation of GM products to campaigning against the institutions which produce the GM products. A strategic move in freeing California and the world in general from transgenic organisms would be to focus on the venues of production concentrated in the state. This type of campaign could resonate well with the public since it would liberate public institutions from the stranglehold of corporations. During these times where skepticism of capitalism has become ubiquitous, a reasonable and strong case can be made for research in the public interest, rather than for corporate profit.

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Introduction

"We will harness the sun and the winds and the soil to fuel our cars and run our factories. And we will transform our schools and colleges and universities to meet the demands of a new age."

- President Barack Obama, Inaugural Address , January 20, 2009[1]

Change is in the air, or at least it appears so. From the "inconvenient truth" about Climate Change to the US presidential campaign won on the promise of change, we are constantly reminded that it is on the way. It is not surprising (but indeed ironic) that an aggressive response would come from the biotech industry to meet the challenge of "change". Biotechnology, that middle-aged man who at 37 would like to don the cape of eternal youth, now embraces the motto of "change" (the first transgenic manipulation took place in 1972).

The past two decades have seen the swift rise and fall of commercialized transgenic plants. The most popular transgenic plants have failed to deliver on their promises of yield increases and cost reductions[2] and have met an intense public and popular opposition in many parts of the world. The biological failures of transgenic crops, coupled with the successful campaigning from public interest groups against them have set the industry in search. A dreaded concept for most, Climate Change is a godsend for the agricultural biotechnology industry as it positions to reinvent itself.

Shortchanged: Biotechnology and the Emerging Climate Market attempts to trace this reinvention, emphasizing the technical strategies used by biotech in its attempt to capture the emerging climate markets. A review of methods used to develop plants for environmental stresses such as droughts and high salinity in soils is followed by a discussion on the developments in biofuel research.

After these two main sections the report briefly looks at some of the recent movement in transgenic research in other areas of environmental relevance, namely, Synthetic Biology, plants as bioreactors, insects, microbes, trees and vaccines. Where applicable, emphasis is placed on information particularly relevant for California and a section reviewing transgenics in California Specialty Crops is also included. The last section looks at some of the web of entities conducting research into climate related biotechnologies in California.

This report attempts to capture the dual face of biotechnology as permanent political and economic fixture of the US-led Western world, while giving a bird's-eye view of the myriad "new" guises in which it presents itself.

What does it mean when a technology works?

Climate Change(s)

Throughout this report the term "climate changes" is preferred to "climate change" when referring to the recent dramatic shifts observed in a long-term analysis of the Earth's weather patterns. There is an unquestionable rising temperature of the globe, but "climate change" implies a singular event and more perversely the possibility of control over the climate which brings with it notions of "fighting and stopping climate change." As detailed in this report, for environmental biotechnology this catch-all term really covers a wide range of activities, from the production of biofuel-ready forests, cellulose-degrading microbes, medical surveillance methods, "climate-ready" crops, and many others. "Climate changes" captures the dynamic and unpredictable nature of weather more accurately. Where the term "climate change" is used it is capitalized to imply the underlying narrative of command and control and it's use as a political device.

Does it mean that a marketable product is developed or does it mean the product actually delivers on its promise? In agricultural biotechnology it is usually the former. Attempts are made throughout the report to identify which of the proposed manipulation strategies are the most promising. But the reader should keep in mind that predicting the future is not an exact science and what peer-reviewed literature is published concerning transgenic transformations is littered with propaganda and science fiction making it difficult to scavenge for truth and reality. As this report is being written, news is breaking of Merck setting up its own peer-reviewed journal under the Elsevier imprint, and it does not take much imagination to know why they would go through such trouble. Throughout this report we are aware that many of the newest environmental interventions may best be understood not necessarily by understanding the molecular biology of DNA, or protein synthesis, but using an analysis of the political, economic and cultural aspects of biotech.

The danger of global ecological catastrophe (from climate changes, pandemics or other lesser known threats) is real and so is the concern. The drive towards change is a positive development for our society in the face of such danger. Yet another danger exists: the danger that while looking for real change we might get shortchanged.

Not a Technology

Even though the term biotechnology has become ubiquitous, genetic transformation is not a technology. Technology means a relatively precise, replicable, predictable and reliable process that matches a pre-determined blueprint and mostly delivers on its promises. The atom bomb or the refrigerator are expressions of technology. Transgenic modifications do not have any of the characteristics listed and they continue to behave outside of expectations. That the products of transgenic manipulation would continue to under-perform, even from a market standpoint, simply stresses this point.

Categories Used in Highlighting

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Throughout the text portions are highlighted in the margins to delineate differences between the proposals of the biotech industry. The categories used are:

I: IMPACT

Possible biological (especially ecological) impacts of the proposal:

high impact medium impact low impact

A: AWARENESS

General public awareness of the proposal:

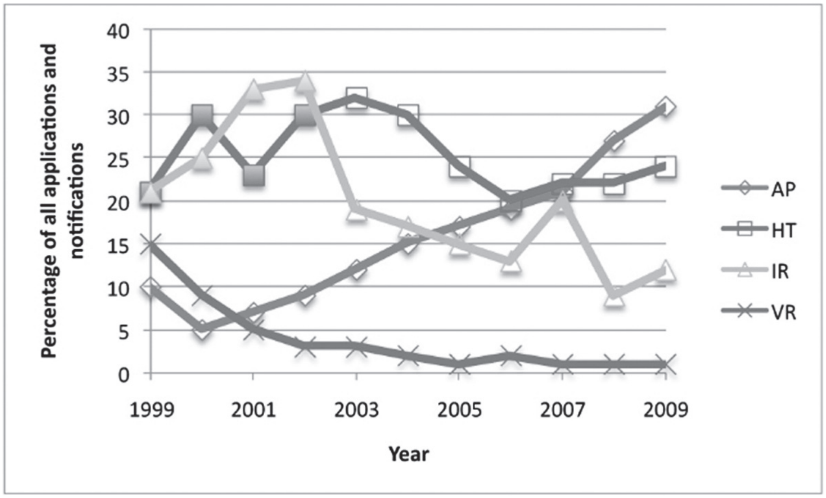
well aware somewhat aware not aware

P: PROPAGANDA/PR

The proposal is based primarily on public relations hype and propaganda rather than real scientific developments:

- based mostly in hype, propaganda and rebranding
- based primarily in 'improvements' to existing techniques
- based on further utilizing existing techniques

GMO Field Trial Trends for the Last Decade



Legend:

Phenotype Categories as Classified by APHIS[3]

AP: Agronomic Properties **HT:** Herbicide Tolerance **IR:** Insect Resistance **VR:** Virus Resistance

This graph illustrates the field trial permit applications and notifications in all of the US, as reported to the Animal and Plant Health Inspection Service (APHIS) in the past 10 years. Certain disclaimers are in order, especially pertaining to the phenotype category classification. There are 11 different phenotype categories that GMO field trials are classified into. This categorization is not strenuous enough and sometimes the same phenotypic modification can fall into different categories. Also greatly ambiguous phenotypes such as "enhanced gene expression" can be categorized under "other." The field trial permit process and associated data can also be deceiving due to multiple phenotypic modifications in a single plant being recorded as separate and superfluous permit requests which are withdrawn or never exercised.

The phenotypic category "Agronomic Properties"(AP) includes many of the phenotype modifications associated with climate change such as drought and salinity tolerance, stress tolerance, water use efficiency, heat tolerance etc. The three other categories are broadly indicative of research along the lines of the majority of currently commercialized GMOs such as "Roundup Ready"ness or Bt protein expression. As mentioned before the lines are blurry and the categorization is less than stringent (for example one can find the phenotype "Lignin Levels Decreased" in the Herbicide Tolerance category). Despite these limitations the above graph still provides a view into research trends concerning GMOs.

We can safely conclude that applications for field trials associated with climate change related phenotypes are on the rise while GMO filed trials for more traditional phenotypes seem to be stagnant or decreasing.

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“Climate Ready” Crops

Even before the ascendance of climate politics to the global magnitude it now holds, (from the teleprompters of western presidents to the boardrooms of transnational institutions, to the fields of monoculture soybeans and palm trees throughout the Amazon basin and South-East Asia) there has been heavy interest in expanding the environmental niches of plants. Biotechnicians have been busy attempting to transform species to tolerate “extreme” environmental conditions: droughts, floods, high and low temperatures, increased salinity and depleted soil nutrients.

Commercial interest in this line of research can be traced at least to the Green Revolution with many plant varieties bred to grow under high-nitrogen input from fertilizers. As a detailed study on one of the initial institutions of the Green Revolution, the Mexico Agriculture Project (MAP), points out “This augmentation in the use of fertilizer, according to MAP scientists, not only served a biological design for greater plant growth, it also served a commercial purpose, namely, as “the keys that unlocked the door to the development of the farm machinery business.””[1]

Similarly, the convergence of molecular biology with the rise of Climate Change politics has opened up both political and market space for the development of new biotechnology products. The changes in meteorological climate have been accompanied by a change in the political climate. But this has been a superficial change and rather than addressing the systemic root causes of ecological catastrophe, the impending global emergency has become a global emerging market. David Noble from University of York, in Toronto has outlined this process in his article *The Corporate Climate Coup:*

“If the corporate climate change campaign has fuelled a fevered popular preoccupation with global warming, it has also accomplished much more. Having arisen in the midst of the worldwide global justice movement, it has restored confidence in those very faiths and forces which that movement had worked so hard to expose and challenge: globe-straddling, profit-maximizing corporations and their myriad agencies and agendas; the unquestioned authority of science and the corollary belief in deliverance through technology, and the beneficence of the self-regulating market with its panacea of prosperity through free trade, and its magical powers which transforms into commodities all that it touches, even life.”[2]

Burning the Book of Life

“Today we are learning the language in which God created life”

-US President Bill Clinton, White House press conference broadcast on the day of the publication of the first draft of the human genome, June 26, 2000[3]

The once fringe idea of human induced climate changes is being accepted concurrent with a growing challenge to previously universally accepted ideas and dominant paradigms in molecular biology. The central dogma of molecular biology, DNA>RNA>Protein and its associated implications of one gene>one protein(>one function) are coming to be regarded as simplistic in the face of discoveries into DNA modifications, regulation and silencing. Epigenetic effects including these molecular events and many others ranging out to the behavioral and environmental continue to be shown to be the rule of the biological game, not the centralized “command-and-control” view of the Central Dogma. This is true especially in regards to metabolic processes such as water uptake, nitrogen uptake and carbon sequestration.[4]

The designation of the DNA-gene as the essential life particle had been established before the completion of the human DNA sequence and it wasn’t only Bill Clinton who likened DNA to the letters in an alphabet and genes to words. Famed co-discoverer of the structure of DNA, James Watson, remarked that “It’s a giant resource that will change mankind, like the printing press.”[5] Undoubtedly, this seemingly simple rhetorical device captured the essence of the DNA-gene’s technical imagination of precision splicing and capitalist development of proprietary patents.

As with current biotechnology products involving herbicide tolerance or insect resistance,

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the narrative of "precise insertions" of single genes conferring phenotypic advantage has not only proved to be scientifically problematic but also even more unrealistic when it comes to modifying plants for "stressed" environments. Metabolic functions of plants (and all organisms) are regulated through a series of cascades, feedbacks, networks and intricate and complex interactions between genetic elements (not only DNA) within cells and abiotic/environmental conditions, changes and fluxes.

To their credit some of the strategies associated with modifying plants for abiotic conditions take these complexities into account and in a sense represent a more holistic understanding of molecular biology. But within the biological sciences, and especially within its commercial offshoots, molecular reductionism still prevails and researchers rarely examine the full life-cycle of an individual plant let alone an ecosystem.

This crisis of the Central Dogma is currently ricocheting throughout the entire field of biotech, and we see it appear in more or less veiled forms in practically every application that is studied in this report.

Marker Assisted Selection

Although not a transgenic method, included here is a consideration of Marker Assisted Selection (MAS) because it is often quoted in discussions about environmental biotechnology. MAS refers to a conceptually simple but technically demanding method through which individual loci (specific locations in a given organism's genome) related to a desired or undesired trait are identified in relation to easily detectable markers nearby in the genome. By analyzing the inheritance of the markers, it is thought that the loci of interest may be tracked, without having to wait until they are expressed. Thus for example a locus thought to be key in providing drought tolerance to a plant may be recognized by nearby marker regions which can be tracked as the inheritance of the drought tolerance is followed from one generation to the next. Multiple markers such as this can be used –at least in theory- to follow multiple loci in a given organism. The latter quality is one that is much vaunted when considering functions that are not determined by a single "gene", but rather by the coordinated operation of multiple genes, for example in so-called quantitative traits (see below).

These methods of identifying traits (quantitative trait loci, associative mapping, selection screening, allele mining and other techniques that fall under the rubric of marker assisted selection) are intensely bioinformatic methods employing microarrays and other high throughput methods of DNA analysis on thousands of plants through generations of inbred lines. Purely bioinformatic, *in silico* simulations of Quantitative Trait Loci (QTL) and signaling pathways are another method that is being employed.[6]

Traits associated with yield and survival under ideal and stressed conditions are quantitative rather than qualitative traits. Both glyphosate tolerance (Roundup Ready) and Cry protein (Bt) production are viewed as qualitative traits where the phenotype is associated to a single gene and degrees of phenotype expression don't exist. Within this still maturing view of molecular biology, quantitative traits lie in contrast to qualitative ones, and are influenced by a large number of genes which "add-up" or "subtract" from a particular trait.

"Current efforts to improve plant stress tolerance by genetic transformation have resulted in several important achievements; however, the genetically complex mechanisms of abiotic stress tolerance makes the task extremely difficult. For this reason, biotechnology should be fully integrated with classical physiology and breeding."[7]

The past ten years have seen advances in the methods used for understanding the genetic influences on complex phenotypes associated with growth, grain size, water uptake and retention, respiration, submergence tolerance (significant for rice growth in regions of Asia effected by flash flooding), aluminum tolerance (in high acidic soils), boron deficiency and toxicity, salt tolerance and other environmental stresses. This has mainly been taking place under the broad category of Marker Assisted Selection.

Mapping and Screening

Marker Assisted Selection (MAS) in its barest of definitions involves screening plant progeny via molecular techniques. These molecular techniques map DNA polymorphisms such as

SSRs, RFLPs, AFLPs[8] and others and associate them with phenotypic charecteristics. It is crucial to note that saying that a plant has been developed through MAS does not necessarily say anything about its transgenic status. Many plants being bred through MAS do not employ transgenic transformations and therefore are not, in the received sense of the term, "genetically engineered" or "genetically modified". On the other hand, some applications employ both MA S and transgenesis side-by-side; an example is the introduction of transgenic markers to assist with selection and the use of MAS-assisted backcrossing to recover transgenic traits in hybrid lines. Therefore when evaluating a proposed agricultural biotech "product" (i.e. plant, animal or microbe) it is important to understand the exact steps that have gone into its development.

The techniques and concepts below fall into the rubric of MAS[9]:

Quantitative Trait Loci are sets or loci within a genome which are known to be related to a specific phenotypic trait of interest in a co-operative manner. These loci may not be responsible for the trait itself, but their proximity in the genome to those loci that are makes them into useful beacons to follow a specific chromosomal region through the vicissitudes of crossings and back-crossings. Biotechnicians hope to construct genome-wide maps of all QTL influencing particular phenotypes. Examples include, those considered by Cattivelli et al. on breeding for water-limiting conditions: i) genetic variation of osmotic adjustment, ii) genetic bases of phenological traits – e.g. "stay green" phenotype, iii) the ability of the roots to exploit deep soil moisture to meet evapotranspirational demand, iv) the limitation of water-use by reduction of leaf area and shortening of growth period; v) isotope discrimination; vi) the limitation of non-stomatal water loss from leaves – e.g. through the cuticle and vii) the response of leaf elongation rate to soil moisture and evaporative demand.[10]

QTL mapping alone does not point to simple transgenesis since it does not necessarily point to a locatable gene that can be transformed into a host organism. But biotechnicians aspire to collect QTL and their associated traits within elite lines by a process of hybrid crosses between elite varieties and individuals with desired QTL, this is called *QTL pyramiding*.

Association mapping is similar in method to QTL mapping yet analyzes genetic markers and phenotypes from collections of diverse germplasms rather than Recombinant Inbred Lines that are needed for QTL mapping.

Selection screening, attempts to identify regions of the genome that have undergone strong selection (i.e. through domestication and improvement) by looking at DNA polymorphisms and the frequency of genetic rearrangements under the assumption that highly desirable traits would be more conserved and patterns will emerge through computational analysis.

Precision breeding is sometimes[12] the name given to a technique that aims to combine transgenesis and molecular screening methods and claims to be able to remove transgenic inserts at the end of product development.[13] Products developed through such methods and claiming to be non-transgenic should undergo an especially rigorous biosafety interrogation.

A FAO Background document written in 2003 is skeptical towards the applicability of MAS: "However, despite the considerable resources that have been invested in this field and despite the enormous potential it still represents, MAS, with few exceptions, has not yet delivered its expected benefits in commercial breeding programmes for crops, animals, forest trees or farmed fish in the developed world."[14]

A review article by Collard and Mackill[15] identifies 11 reasons why Marker Assisted Selection has not delivered on its promise:

- MAS is still at its early stages of development,
- the proprietary nature of marker mapping research in plants with commercial value prevents collaboration,
- low levels of reliability and accuracy due to large confidence intervals in QTL studies,
- insufficient linkage between a marker and the actual gene or QTL,
- limited differences (polymorphisms) between markers,
- difficulties in identifying QTL amongst different genetic backgrounds,

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- the different phenotypic outcomes QTL has in different genetic backgrounds through interactions with other loci or epistasis,
- unexpected interactions between QTL and the environment,
- the high financial cost of Marker Assisted Selection,
- an "application gap" between laboratory research and plant breeding institutes which engage in field station associated research,
- a "knowledge gap" between molecular biologists and plant breeders.

Transgenic Modifications

As outlined above an organism's response to environmental fluctuations are understood to be an incredibly complex process not affording the easy solution of identifying a specific stress-related gene and transforming a target species, but there are still some transgenic proposals on the table. These transgenic proposals often involve inserting or targeting multiple genes (gene stacking)[16] related to a stress-response, attempts at tissue localization and stress-induced promotion of the transgenes. A review article from November 2007 has this to say regarding the transformations of plants for abiotic stress:

"However, that approach (single-gene transformations) has overlooked the fact that abiotic stress tolerance is likely to involve many genes at a time, and that single-gene tolerance is unlikely to be sustainable. Therefore, a second "wave" of transformation attempts to transform plants with the third category of stress related genes, namely, regulatory proteins has emerged. Through these proteins, many genes involved in stress response can be simultaneously regulated by a single gene encoding transcription factor, thus offering possibility of enhancing tolerance towards multiple stresses including drought, salinity and freezing." [17]

The complexity of the genetic factors that go into environmental stress is acknowledged yet there is still a drive for a so-called "silver bullet" which will play the role of central command over the complexity. Different from the majority of transgenic crops on the market today, engineering for regulation, and stress-response in general, requires an approach which is not constitutive, where the modification is not effective throughout the plant's life cycle and in all tissues (see below for a discussion on metabolic costs). For this reason genetic promoters specific to abiotic stress responses have been sought.

These transgenic aspirations are likely to fail and "The progress in actual production of transgenic plants with improved abiotic stress tolerance has been slow"[18] but for the purposes of this report a cursory review of the target gene families are in order.

"Single Action Genes": Genes assuming to have single and static functions and identified as candidates for abiotic engineering include genes found to be associated with:

- osmotic stress (a disruption in the functional equilibrium of intra and extra cellular metabolites and ions which cause movement of water across the cell membrane) and the related production of osmoprotectants (a variety of organic compounds, sugars and alcohols countering the effects of osmotic stress),
- detoxification of anti-oxidents against accumulated reactive oxygen species (ROS) that are damaging to nucleic acids, proteins and membranes,
- membrane transport to achieve cellular ion homeostasis (a major approach for engineering salt tolerance) ,
- late embryogenesis abundant (LEA) proteins,
- and heat shock protein genes.

"Regulatory Genes" or Transcriptome engineering: A slightly more promising but still reductionist approach is to enhance stress tolerance via a genetic transformation for a stress inducible transcription factor. Transcription factors which set off cascades of reactions such as dehydration responsive element binding proteins (DREBs) and C-repeat binding proteins (CBFs (C-repeat Factors)) have been studied extensively in the model organism *Arabidopsis* and engineered in tomato, wheat, tobacco, rice, alfalfa and petunias.[19] Signal transduction factors that control downstream events have been engineered in tobacco, rice, cotton and canola. [20]

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Patenting "Climate Genes"

Naturally the emphasis on the coming age of Climate Change has motivated the increased patenting of genes associated with stress response regulations . The ETC Group has recently published a report detailing the patenting of genes associated with mechanisms regulating responses to abiotic stress. According to them "BASF, Monsanto, Bayer, Syngenta, Dupont and biotech partners have filed 532 patent documents (a total of 55 patent families) on so-called "climate ready" genes at patent offices around the world."[21] Many of the genes referenced above remain in the proprietary crosshairs of biotech firms.

Metabolic Costs

An often mentioned and irresolvable dilemma in producing plants to tolerate environmental stress is the shifting of metabolic costs from processes related to agricultural products (such as fruit/seed emergence and development) to expensive maintenance, stress-response and detox processes. To deal with this problem research has gone into looking at promoters associated with stress responses and other non-constitutive genetic engineering strategies.[22] Even if research was able to produce agricultural plants to withstand extreme environments it is extremely unlikely that these plants would be productive and offer satisfactory yields under diverse environmental conditions.

Ecological Effects of Crops via Gene Flow

For the purposes of looking at the potential gene flow consequences arising from crops engineered for abiotic stress we will assume that the strategies outlined above are successful in creating these agricultural products.

The effect of gene flow is related to both the amount of cross hybridization occurring between members of the same species, close relatives or extremely distant ones (through Horizontal Gene Transfer) and the advantage or disadvantage conferred by the phenotypes associated with the particular gene.

In the case of genes conferring advantages to abiotic stress the effect of hybridization will influence the environmental niche the recipient can occupy. Assuming that crops are successfully engineered for changing climate and soil conditions (again a highly unrealistic assumption) any gene flow will render the recipient more competitive within such a particular ecosytem. Perhaps the most relevant scenario in this case would be hybridization and gene flow to a wild and weedy relative, creating greater costs for agricultural producers.

Concerns around transgenic flow have been ever present since the first suggestion of GM technology in agriculture. Some of the current work in GM agriculture is specific to lessening or preventing gene flow (so called Genetic Use Restriction Technologies or GURTs) such as chloroplast transformations (chloroplasts are only inherited maternally), male sterility (where pollen isn't produced), seed sterility (seed produced is not viable), self-pollination (pollen is only compatible with self), apomixes (fertilization without pollination), genome compatibility (specific transgene introgression locations render the genome incompatible with others), and transgenic mitigation (offspring from transgenes are less fit).[23]

The Climate is not in Chaos, Climate *is* Chaos

"Because stress conditions, such as salinity and drought, vary depending on local climates and geographical features, the fine tuning of gene activities will be required for practical application in each area."[24]

A telling quote form a research review paper (in fact optimistic about some of the above outlined efforts) which points to the dead-end of the research initiatives and product development. Apart form the immensity and cost of such "fine tuning of gene activities" for each climactic condition (naturally an intrinsically slow evolutionary process, impossible to accelerate with molecular tools) there also lies the difficulty in predicting climate events which create abiotic stresses. Climate models that have signaled human disturbances and brought about the fervor over "climate ready crops" and "more crop-per-drop" are employed for making large-scale and long-term global assessments and somewhat ironically predict erratic, chaotic and unpredictable climate events.[25]

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This level of indeterminacy does not bode well for crops that have been tailored for particular climates in the lab. It is useful to remember that one of the original insights into Chaos, the study of dynamic unpredictability was one associated with weather. This was the basic idea that a butterfly flapping its winds in one part of the world could eventually set in motion the events that would cause a hurricane in another, distant, place.

Of course, since climate systems are impossible to replicate let alone predict, field trials for efficacy might very well be useless and current evaluations have not even met the needed scientific scrutiny. The post-transformation evaluations of plants engineered to resist abiotic stress have come under fire, even from researches who regard transgenesis as an attractive option. Most research into drought tolerance has disregarded yield in field trials and solely scored plants for survival.[26] For example "Regarding salinity, most of the evaluations reported so far have been carried out at the seedling stage, although this type of evaluation has been reported to have little correspondence, if any, with how plants will later perform under salt stress." [27]

The emphasis on genetic engineering observed in the first generation of agricultural biotech products appears to be waning when it comes to plants produced to withstand abiotic stress. The reasons for this are twofold, first, and primarily, the public reluctance to embrace GE food crops and the venomous opposition to it and secondly the poor performance of transgenisis, especially in regards to complex traits such as yield under environmental stress.[28] Because of these two factors it is likely that new varieties of crops marketed as drought or salinity tolerant (or other products claimed to withstand environmental extremes) will be preferred to be developed via Marker Assisted Selection rather than traditional recombinant DNA methods of plant transformation.

Different ideas and examples of appropriate, equitable, liberating and ecologically sustainable practices and even technologies do exist in the face of climate changes but they have not been sufficiently considered or researched.[29] Instead agricultural research continues, as it has for half a century within the purview of profit-centered interests and, therefore, with product development aimed at this same end, even if by different means such as marker assisted selection.

Table 1. *Modifications used in developing plants tolerant to abiotic stress (continued on next page)*

	Reasoning	Method	Promise	Comments/Analysis/Critique
Modifications				
Single-Insert Transgenics	The original, "Silver Bullet" idea: one gene-one function. Single DNA inserts endow the recipient with a new peptide or protein which –it is hoped- produces a function. By finding the crucial variants of certain enzymes from other organisms, such silver-bullets would provide higher tolerance of GM plants to environmental stress.	A DNA sequence is inserted for a specific protein. Although the method implies a claim of minimal intervention, no "single-insert" is possible: transgenic constructs ("Inserts") contain DNA sequences from several sources, and become inserted in various arrangements at various points of the host genome.	The biology of responses to abiotic stress are much more complex to be solved with single – insert transgenics. This is already acknowledged widely by those who are in the midst of developing climate engineered crops.	Growth during conditions of environmental stress is driven by so-called Quantitative Traits involving many genes and epigenetic influences. Because there are interactions involved, this generates complexity which cannot be defined simply as a sum of additive parts. It is highly unlikely that earlier transformation methods used to produce "first generation" GM products such as Roundup Ready or Bt toxin producing plants will succeed in producing plants engineered for abiotic conditions.
Stacked Transgenes	Combining the functions of more than one single insert has become the common-place solution for the obvious failure of single inserts in dealing with complex functions, such as needed for abiotic response management.	"Stacking" (multiple insertions) does not represent a break from the One-Gene-One-Function paradigm. Multiple DNA sequences are introduced into a plant by sequential single-insert manipulations, or by the use of an already-transgenic parent lineage to which a new DNA insert is incorporated.	While still unlikely to result in products that "work" the promise is marginally greater than single-insert transgenics since these transgenic plants will have modifications relating to more than one gene.	Quantitative Traits involved in abiotic stress management are determined by a concert of various cell and organismic functions. The genetics behind such inter-related traits is highly choreographed, so that the addition of simple elements in any order does not mean that the resulting plant will display the "designed" qualities. Only breaking from the One-Gene-One-Function paradigm would begin to offer some promise, but then patenting and commercialization is not compatible with such a paradigm.

	Reasoning	Method	Promise	Comments/Analysis/Critique
Modifications				
Marker Assisted Selection	a) Certain traits are contingent on the particular environments and therefore not readily observable as phenotypes during breeding experiments b) Growing many generations of plants to maturity is too time consuming and/or costly for biotechnology ventures.	Quantitative Trait loci in a plant's genome are "mapped" by following their position relative to recognizable "beacons" or markers. The key here is scale; different from the single-insert approach, in MAS as many markers are identified in many cells from many different progeny. Microarrays can facilitate the simultaneous genetic mapping of loci on hundreds of individuals and recent IT applications can crunch through the data effectively and quickly. Ultimately, with breeding practices, loci can be "collected" on a hybrid plant, hypothetically conferring an advantage.	Advocates of these particular methods point to the lessening of time needed for screening generations of plants. Another argument heard in favor MAS techniques is that by looking at molecular data (nucleic acid sequences etc.) one can select for phenotypes not observable or measurable at that time. MAS is often portrayed as a mixture between traditional breeding and molecular biology. There are commercialized MAS crops and are already some inklings of product development through MAS for abiotic conditions and it is highly likely that varieties purporting to mitigate environmental stressors will be marketed.	Marker Assisted Selection of quantitative trait loci goes a step further in the right direction by accepting the complexity of genetic factors. But it still remains locked in the view of the genome as a static arrangement of molecules whose phenotypic outcomes can be predicted. Our evolving understanding of genetics and the dynamic character of the genome, especially in respect to environmental signals, does not bode well for a biology locked in the reductionist realm. On top of this, and applicable in general to this table, is the erratic unpredictability of climate systems (including secondary environmental responses to climate changes). Careful tailoring for climactic conditions does not necessarily expand the plant's niche but limits it to another set of conditions.
MAS + Transgenics	Single nucleotide polymorphisms or other markers are not robust enough for selection. Transgenic traits can be selected faster	Markers can be introduced into the genome artificially to assist in both QTL mapping and MAS. Transgenic traits can be recovered in hybrid parents in backcrosses taking less time through MAS.	There have already been transgenic plants which have used MAS methods. The artificial introduction of markers holds the potential to speed up the process even more yet the public reluctance to accept GM might push biotech companies to not prefer this method.	It is probable that the debate over transgenics will become convoluted with the increased prominence of crops engineered through marker assisted selection. It is important to recognize that MAS is not genetic engineering. But it is still necessary to scrutinize crops claimed to be produced through MAS since many times MAS and transgenisis take place together and in relation to each other. This will require higher biosafety literacy amongst advocacy groups to cut through smoke and mirrors in order to determine the exact process through which a certain plant product was developed

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Genetic Engineering for Biofuels "GE Free Fuel"?

"In 2006 and 2007, the emerging biofuels industry was hit by a "perfect storm" – an unprecedented confluence of social, political, economic, and environmental factors that point to a promising future for the biofuels market."

– John Doeerr, Partner, Kleiner Perkins Caufield & Byers (Earnst and Young, *Beyond Borders Biotech Report*)[1]

Legislative action for the promotion of biofuels has been rolled out following a "perfect" and very convenient alignment of events, some of them environmental, some of them biological and many of them political. Even though biofuel efficiency and carbon emission reductions predicted with their use has been sufficiently critiqued[2] the US federal government set a goal of a %30 replacement of US petroleum by biofuels by the year 2030.[3] The hype around biofuels was compounded due to successive mentions by George W. Bush in his state of the union speeches. This trend continued and further solidified with Barack Obama's election to the US presidency. Obama's appointments such as Secretary of Agriculture Tom Vilsack (former Iowa Governor), Secretary of Interior Ken Salazar, Steve Chu (former head of Lawrence Berkeley National Labs) as Energy Secretary and Steve Koonin (former BP scientist) as Undersecretary of Science, all of whom are staunch supporters of biofuels and transgenic options for biofuel production, point to the officially designated road ahead.[4]

Ethanol production from corn comprises the vast majority of liquid fuels derived form plants in the U.S. In 2006 there were 131 ethanol biorefineries in the US with an estimated increase of 72 more, together this is predicted to allow a capacity of 13 billion gallons of ethanol per year.[5] Propagandists for ethanol aspire to increase this to a mind-bogglingly unrealistic 150 billion gallons per year by 2050 with the methods outlined below.[6] Against this backdrop of political optimism, the reality of ethanol production plants is that they operate only because of wide margins of subsidization; even with these, many companies are currently being forced to fold or to reduce dramatically their production plant, and their share value is extremely low despite efforts to increase the tax-payer support to the highest levels. [7]

"In the pantheon of well-intentioned governmental policies gone awry, massive ethanol biofuel production may go down as one of the biggest blunders in history. An unholy alliance of environmentalists, agribusiness, biofuel corporations and politicians has been touting ethanol as the cure to all our environmental ills, when in fact it may be doing more harm than good. An array of unintended consequences is wreaking havoc on the economy, food production and, perhaps most ironically, the environment."[8]

In a simplified summary, the current ethanol production process consists of the hydrolysis of starch from grain into sugar and the fermentation of the sugar into ethanol. A number of problems have arisen from this particular route of biofuel production. These problems are intertwined with the political economy of agricultural production and the biological limitations of biofuel generation.

Before delving into these biological limitations, the market driven food price fluctuations under pressure from biofuel production deserves a brief mention. In 2007-2008 food prices skyrocketed around the world. The prime example of this was the dramatic rise of the price of corn tortillas, in Mexico, where corn is a staple of households. Mexico was not an anomaly and food prices jumped in countries across the world resulting in hunger-driven riots in Haiti, Bangladesh, Egypt, US cities and many others.[9] Amidst a multiplicity of causes related to global finance capital and ecological factors, the rise of the ethanol economy was identified as a leading culprit. The United Nations has likened the effect of biofuels on food prices to "a crime against humanity" and has called for a freeze on all investment in this sector.[10]

Next Generation Cellulosic Biofuels

Pushing biofuel development towards cellulosic feedstocks (using the majority of the plant biomass of biofuel crops) and away from starch (grain from crops that could be food or feed) based ethanol has been proposed as one solution to mitigate the effects that biofuels have on food prices. The move towards cellulosic biofuels also comes with the promises of increasing cost efficiency (more biomass per feedstock plant) and carbon sequestration on top of purportedly resolving the conflict of food vs. fuel.

Amongst new crops identified as next generation feedstocks (for example trees such as eucalyptus, loblolly pine, willow, silver maple and perhaps most significant for California, hybrid poplar[11]) perennial grasses such as switchgrass and miscanthus stand out and are at the center of large scale research collaborations.[12]

There are two main avenues of inquiry into implementing genetic engineering techniques in relation to biofuels from plants. The first is in regards to increasing feedstock obtained per hectare while the second is in regards to the processing of the biomass.

Ethanol production from cellulosic ethanol is highly costly due to several biological characteristics of plants. The polysaccharides cellulose an hemicellulose are part of the primary and secondary cell walls of plants. According to Sticklen, depending on the plant species 15-30 % of the primary and up to 40% of the secondary cell wall is composed of cellulose and hemicellulose constitutes 20-40% of total cell wall polysaccharides.[13] The pretreatment of lignocellulose, in the words of the cellulosic ethanol industry "cooking the cake," is an extremely costly step of heating and chemical treatment and has been identified for transgenic strategies.

Therefore from a general standpoint the bulk of the genetic modifications under investigation are concerned with cell wall degradation, accessibility and hydrolysis. This is the same cell wall that provides both the structural stability of all plants and its principle physical barrier against diseases and pests. In this regard genetic modifications associated with the cell-wall present a new terrain of ecological effects and associated dangers.

Increasing Biomass

Naturally all research into increasing the net biomass yield of crops is relevant to research looking to optimize biofuel production. There is a great deal of overlap in this field between previous agricultural biotech research and the more recent Climate Change induced biotech research. Yield increase research in feedstock crops for cellulosic ethanol focus on increasing plant cellulose content. Current research is looking into specific plant growth regulators and shifting metabolic growth expenditure towards cellulosic material rather than starch.

Bioinformatics is heavily used in this line of research as well: "For example, even in studies of model plants such as *Arabidopsis thaliana*, most of the cellulose biosynthesis pathway enzymes have been identified based on hypothetical modeling, without confirmation that they actually have roles…"[15] There are still many gaps in our understanding of cell wall biosynthesis and significant genotype nonspecific discoveries are yet to be made with advances only in a few cultivars of certain feedstock candidates.[16]

On top of this general knowledge deficiency, research into many of the new feedstock candidates such as switchgrass and mischantus are still at their infancy. "The newly emerging biomass crops such as switchgrass and *Mischantus* are essentially wild populations, and like food and feed crops they require years of traditional breeding and related molecular approaches such as genetic markers and genome mapping."[17]

Microbes

Many of the enzymes associated with cellulosic biofuel production such as cellulases, hemisellulases and ligninases are found in cellulolytic microorganisms such as fungi and bacteria. Considerable amount of research is being done into engineering genes associated with cell-wall degrading enzymes into well studied microbes such as the bacterium *E. coli* and the yeast *S. cerevisiae* for industrial production of enzymes in fermentation vats.[18]

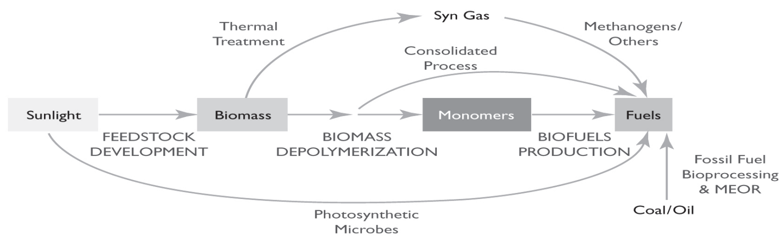

Figure 1 *Routes of energy production to be explored in EBI. All caps indicate programs.*

Image 1. *Figure from the Energy Biosciences Institute final contract outlines the main steps involved in producing ethanol from cellulosic material. All of the steps except thermal treatment are being considered for transgenesis.*[14]

Microbes are at the crux of the final fermentation step in converting sugars into ethanol and therefore an attractive and relatively simple target for genetic modification. Research conducted by the Joint Bioenergy Institute and others is seeking to expand the repertoire of fermentable sugars by microorganisms and they are moving towards engineering *E. coli*, *S. cerevisiae* and the archean *Sulfolobus solfataricus* to improve their tolerance to conditions such as toxic ethanol levels during bioethanol production.[19]

Two for the price of one? Feedstock Bioreactors

The major step in cellulosic ethanol production is the hydrolysis of celluloses and hemicellulose to produce fermentable sugars. The hydrolysis of these two polysaccharides is carried out by the enzymes cellulase and hemicellulase respectively. As mentioned above the state of the art in cellulosic ethanol production performs this major step by producing these enzymes through microorganisms grown in large growth vessels. This is one of the most costly steps of cellulosic ethanol production. One of the proposed methods being worked on revolves around the production of these enzymes within the plant used as feedstock (sometimes this is referred to as *in planta* production). The research aims at utilizing recombinant DNA methods to transform feedstock plants with microbial genes associated with enzymes that hydrolyze cellulase and hemicellulase. This would theoretically streamline the ethanol production process and overcome a costly step.[20]

One of the mysteries, caveats or extreme dangers (depending from which side one approaches the problem) of the *in planta* production of hydrolysis enzymes is the potential premature hydrolysis of cell wall polysaccharides before ethanol production. The spread of transgenes engineered to facilitate cell wall degradation through populations via gene flow presents a severe risk. Horizontal Gene Transfer (HGT) events could potentially create microbes that are more efficient in attacking plants, thus inducing enhanced pathogenesis. There are various strategies biotechnicians are pursuing to prevent this which seem extremely tenuous such as pH and/or temperature incompatibility between the cell cytoplasm or organelles where the enzymes would be produced and the optimum working conditions of the enzymes.

Lignin Removal

Another costly step in the production of cellulosic ethanol that is being tackled through genetic engineering is the removal of lignin from the cell walls. Lignin is a major barrier to the conversion of cellulose and hemicellulose into fermentable sugars as it reduces the accessibility of hydrolysis enzymes to the polysaccharides. Conventionally lignin is removed through costly heating and/or alkali treatment. Genetic engineering proposes to modify the chemical structure of lignin in a way that would reduce the cost of its removal, but the biochemical pathway of lignin production is still not completely understood, and even less likely to be engineered any time soon. Currently there are efforts to down regulate lignin biosynthesis through the use of various transcription and translation inhibitors such as antisense oligonucleotides and RNA interference.[21]

The engineering of novel types lignin to reduce the recalcitrance of lignocellulose carries great risk at the ecosystem level. Lignin strengthens cellulosic material in order to form the cell wall and provides a crucial defense against pests and pathogens. Gene flow from plants with novel types of lignin has the potential of spreading and compromising the resistance of plants against pathogens throughout ecosystems. Such evolutionary-level manipulations have never been seen in ecology except in the homologous process of exotic species introductions into ecosystems. From what we know of invasion ecology, the consequences of this type of effect can be large and catastrophic.

Biodiesel from Microalgae

Currently biodiesel production rides on plant and animal oils. In the United States the primary source used for biodiesel are soybeans but other sources of commercialized biofuels include canola oil, animal fat, palm oil, corn oil and waste cooking oil.[22] Best case calculations of yield, oil recovery and transesterification to produce biodiesel from major oil crops point to extreme land demands of close to a ¼ of arable US land to meet 50% of the fuel consumption and are unfeasible.[23] For this reason and to answer criticisms of food vs. fuel several companies including California based Aurora Biofuels, are attempting to develop biodiesel from genetically engineered microalgae, a unicellular photosynthetic organism which lives in aquatic environments. Claims are being made along the lines of a 300 fold increase with a 300 fold decrease of land needed in comparison to soybean based biodiesel.[24] "Encouraged by high oil prices and the push for alternative fuels and carbon trading, more than 100 such algae-to-fuel companies have popped up worldwide, mostly in the last couple of years, say industry experts. But, not a single commercial facility has been built, and an eagerness to be the first, plus the enticing investment along the way, has encouraged some entrepreneurs to overstate their capabilities."[25] and data is being extrapolated inappropriately for large-scale production from small-scale facilities run by algal biofuel companies.[26]

According to Rosenberg *et al.* "Over the years, algal biotechnology companies have brought a number of products to the market, ranging from aquaculture to specialty chemicals. Currently the development of pharmaceutical compounds and biofuels is the priority of the industry."[27] Microalgae is a unique candidate for biofuel production due to their photosynthetic ability, high oil content and manageable cultivation and although genetic engineering of microalgae has been identified as a major cost reducing step, research into this realm is still at its infancy and genetic modification of microalgae has received little attention until recently.[28] Part of the reason why research has been progressing slower than desired is due to the particular resistance algae has shown towards transgenesis by genetic silencing through RNA interference.[29]

The ecological consequences of genetically engineered microalgae will be relational to its environmental release. The current proposals for their industrial scale production are open raceway ponds and closed yet transparent photobioreactors.

Other biofuel options in development but which have not received as much attention include, biomethanol, synthetic natural gas (syngas) and biohydrogen.

Synthetic biology (see next section) is being presented as the newest frontier in the biotech imagination and companies such as Craig Venter's Synthetic Genomics claims to eventually be able to construct synthetic genomes and microbes for efficient biofuel production such as ethanol, butanol or biodiesel. There is considerable clamor around metabolic engineering and synthetic biology and "synthetic biologists are looking to either modify existing organisms or create from scratch microorganisms with minimal genomes and therefore with a minimal set of metabolic pathways."[30] This is a farfetched idea that is currently far from realization.

The latest OECD-FAO Agricultural Outlook report points to at least a doubling of bioethanol production by 2017 and even larger increases in biodiesel production.[31] It is most likely that already existing and future biotechnology products will be integrated into this emerging and speedily growing market.

Ernst & Young, a venture capital consulting company, has compared the emerging biofuel market to biotechnology in its early days "when the industry was characterized by tremendous potential amid considerable uncertainty."[32] Perhaps what will become the most crucial factor in determining the development of biofuels will be its competitive advantage with traditional fossil fuels. Currently biofuels are only profitable due to intense government subsidy programs and the whole project might disintegrate due to budgetary decisions, fossil fuel price fluctuations and reprioritizations.

Table 2. *Cellulosic Ethanol and Transgenics*

			Reasoning	Method	Promise	Comments/Analysis/Critique
Transgenic Plants used as feedstock (For transformations directly related to post-harvest processing see below)			Traditional arguments for GMO plants, such as yield increases for greater feedstock biomass, herbicide tolerance, insect resistance etc.	Conventional recombinant DNA methods used to carry out transformations of plants.	Different plant species are being proposed as feedstock for biofuel production (switchgrass, mischantus) and it is likely that there will be an increase in environmental releases of populations with modified genomes (growth increases and shifting metabolic processes away from starch production and towards cellulose production.) But due to the near impossibility (financial and biological) of cellulosic fuel production we do not foresee commercial applications of cellulosic biofuel feedstock in the near future. For starch-based biofuels, GM feedstock production is likely to continue with possible new transgenes	Industrial agro-biofuels are likely to continue to be produced in high quantities and heavily subsidized by the government under the new politics of climate-related regulations. Biotechnology firms could drastically shift from food and feed markets, due to consumer rejection, and into feedstock markets. Since fuel is not ingested into the body certain critiques of GM can thus be avoided.
Post -Harvest Processing	**Enzyme Production**	*Contained Production*	Enzymes associated with biofuel production from starch and cellulose, mostly found in fungal species, must be industrially produced for commercial scale applications.	Conventional recombinant DNA methods used to carry out transformations of microorganisms	Enzyme production from genetically modified microorganisms is already taking place at a routine level. Transformations for enzymes active in particular conditions (temperature, pH etc.) are likely to continue.	Categorically, contained applications of transgenic organisms are safer than environmental releases. Of course there is always the possibility of infrastructural failure, mistakes, natural disasters and other factors that can cause an inadvertent release of one or many GMOs. Large-scale commercial applications, even if contained, are highly likely to have some level of biological leakage due to lax and insufficiently regulated biosafety practices. This is in spite of the possibility that the particular GMOs might have dire environmental consequences unforeseen due to perceived containment.
		In planta *bioreactor*	Enzyme production is a costly step in the production of biofuels	Transform feedstock plants to internally produce the necessary enzymes required for their processing.	Syngenta has already produced an alpha-amylase producing corn variety for ethanol production from starch (1st generation biofuels). There are also proposals for the *in planta* production of cellulases, hemicellulaces and ligninases although these are sufficiently more difficult due to the poorly understood enzymatic pathways.	One of the dangers of the *in planta* production of hydrolysis enzymes is the potential premature hydrolysis of cell wall polysaccharides before ethanol production. The spread of transgenes engineered to facilitate cell wall degradation through populations via gene flow presents a severe risk. Horizontal gene transfer events could result in novel microorganisms that are efficiently able to breakdown plant matter.
	Lignin Removal		Conventionally lignin is removed through costly extreme heating and/or chemical processes	Genetic engineering to modify the chemical structure of lignin to decrease the cost of its removal	The biochemical pathway of lignin production is poorly understood and it is unlikely that commercialization will take place in the near future.	Gene flow from plants with modified lignin in the environment poses the threat of morphologically deformed plant populations. Lignin is also crucial in the plants defense against pathogens and modified lignin structure raises the possibility of plants more susceptible to pathogens.

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Synthetic Biology

The brainchild of a few engineers from MIT, Berkeley and their satellite companies and organizations (e.g. the little-known but influential, Berkeley-based Molecular Sciences Institute), Synthetic Biology is a term that may well be attributed specifically to Jay Keasling (Berkeley/BP/Amyris/Codon Devices) and Drew Endy (Stanford/MSI/Codon Devices). The term has spawned a very well-endowed series of companies which form one of the most important keystones of the current drive for a "bioeconomy".

Despite its financial, conceptual and political dominance, the term Synthetic Biology (or SynthBio) does not lend itself to simple definition. The best that can be offered is simply that Synthetic Biology is Genetic Engineering by a different name. In practice, SynthBio uses the tools of transgenesis to attempt to produce living, reproducing organisms with "desirable properties", i.e. a phenotype which may be deemed useful by some audience or the other. Instead of the "traditional" method of genetic engineering in which one or a few sequences of DNA are introduced into an organism, SynthBio attempts its goals through the simultaneous introduction of many sequences of DNA into an organism. The promises of such a practice are as wide as there are diverse imaginations among audiences as to what may be considered useful: "greener" fuels, cheaper medicines, personalized medication, environmental clean-up ("remediation"), end of hunger, "carbon-free" economic development, more deadly and more stealthy weaponry and so on.

Like Golden Rice, in Michael Pollan's terminology, SynthBio is a "rhetorical technology" which succeeded in bringing fresh investment into the flaundering biotech industry: venture capital and governmental subsidies flow into this field through many different avenues ranging from research financing agencies (USDA, NSF) to local, state and federal support. In this regard, SynthBio has something in common with nano-technology, in that the term is enough to revamp the image of industrial processes that may not have been very successful commercial ventures without their new image. Of particular and unique interest is that SynthBio also attracted large corporate interest, most notably the participation of Monsanto and BP in various ventures in the field. The San Francisco Bay Area, particularly around Berkeley, is the epicenter of these developments.

SynthBio, as a concept, proposes to "create" organisms "from scratch" by assembling "biological parts" according to a pre-determined blueprint. This idea borrows directly and verbatim from fields that belie the conceptual background of the main proponents, who are in general computer engineers, chemical engineers and even civil engineers by training. Thus SynthBio claims that organisms are nothing but "DNA circuits" operating a "code" on a given "operating system". The claimed power of this approach, which does not describe any specific activity or manipulation, is that it does not have to deal with the "messy background" of organisms produced through normal evolution. "Writing" "clean code" –the claim goes—makes possible what was not possible through "normal" or "traditional" genetic engineering.

There are three main problems with this idea:

•It is not possible to produce living forms from inert reagents, and there is nothing in the most remote horizon that seems to be able to change this. What SynthBiologists call an "operating system" is in reality not a raw set of pieces of machinery waiting for an order from the central "code" to jump into operation (as is the case with computers). Instead, the "operating system" (sometimes also referred to as the "platform" or the "chassis" for SynthBio "constructs") is perforce a living and working organism.

•It is not possible to predict the outcome of SynthBio transgenic manipulations from first principles. A "blueprint product" scheme, the basis of any manipulation in engineering is also not possible. There are several reasons for this impossibility, but perhaps the most fundamental is the recursive interactivity and nested structure of living systems. In other words, living "things" have basic complexities which can be shown to render them and their functions unpredictable, therefore intractable through a "blueprint product" approach. Recursive interactivity over time

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and space (i.e. different parts in the complex system influence each other reciprocally across distances that range from the molecular to the geographical, and across time ranging from the millisecond to the millennium scales) ensures that no predictability is possible, as in turn predicted by chaos theory, among others.

•It is not possible to use DNA as "code", much less as "instruction manual" for the living organism (the "operating system" of the SynthBiologist) to function. This idea, heavily indoctrinated into young minds and maintained through superficial treatment of biology throughout our culture, is difficult to grasp initially. But biological reality is that DNA does not "contain" the "code" to "build-up" living organisms. While it is true that much interesting and important heritable information dwells on DNA molecules, equally important information is "contained" in proteins (e.g. polymerases needed to build up proteins, to build up DNA), in RNA (especially the universe of microRNAs which is only now being discovered and which throws a very large challenge to SynthBio).

We have witnessed in molecular biology a silent revolution in the last 10-15 years when many more genomes of various organisms have been disclosed for our research. This research has shown that a large proportion of DNA in many organisms is not compliant with the "Central Dogma of Molecular Biology", which is one important cornerstone in the SynthBio edifice. Perhaps it is because these discoveries are so damaging to a whole field, to an industrial sector and to the very idea of "progress" as defined in the SynthBio program that this dramatic change in understanding has evaded general, public awareness.

The failure of the concepts behind SynthBio can be dramatically illustrated by the recent expiration of one of the two flagships of the industry, Codon Devices of Cambridge, Mass. Post-mortem analysis is difficult to do in this case, because all participants have proven extremely reluctant to make any statements whatsoever; even the website of the company remains open at this time (April 2009) and offering jobs, despite the fact that there is no company behind it.

In any case, the limitations and risks of transgenesis apply to SynthBio interventions as much as they applied to prior attempts to "engineer" living organisms through "traditional" genetic engineering.

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Plants as Bioreactors: Nutritionally Enhanced Plants and Pharma Crops

Tweaking nutrient production pathways and inserting transgenes that either upregulate metabolic production or facilitate the production of novel pharmaceutical products (such as vaccines or therapeutic enzymes) has been a longstanding proposal of the biotech industry. This family of biotech products has been exemplified by the emergence of GoldenRice, marketed as a therapy for Vitamin A deficiency. The principle critiques against these products have been that the nutrients can be obtained from naturally occurring plants and that gene flow and contamination associated with such bioreactive substances could result in toxicity and alergenicity. Below are some samples (and by no means comprehensive) of nutritionally enhanced crops:

• Soybean developed by Pioneer Hi-Bred and modified for Increased levels of monounsaturated fatty acid and decreased levels of polyunsaturated fatty acids has recently completed a consultation with the FDA.[1]

• Potatoes are being genetically engineered for higher nutritive value.[2]

• Tomatoes have been engineered to produce flavonoids and anthocyanins that have anti-oxidant properties (regarded as reducing the risk of cardio-vascular disease). This product, although not commercialized has already come under popular critique[3] after being publicized. There is also a proposal for the alteration of tomato aroma by manipulating the levels of volatile aromatic compounds such as linalool[4] and modification for B-carotene (similar to golden rice) and other cartenoids.[5]

18 field trial permits have been taken out in the past 2 years, with many in California, by California biotech company Arcadia Biosciences for an altered oil profile of *safflower*. Arcadia is conducting research into producing safflower oil with high gamma-linoleic acid (GLA) which is planned to be marketed as a weight loss dietary supplement and anti-inflamatory agent. Arcadia is proposing GM Safflower oil as a new alternative for omega 6 fatty acids. The biotechnology industry has been able to respond to health related critisicms of transgenic material in oils by claiming that oils are free from DNA.[6] Despite the fact that this claim has been scientifically disputed and proven otherwise[7], a dietary supplement oil from GM crops might be the ideal candidate for a commercialized, nutritionally enhanced plant.

According to a review published in *The Journal of Medicinal Food* "the GM enhancement of a metabolic pathway by the overexpression of genes for that pathway can have unpredictable consequences in the form of synthesizing a toxin" and "compounds structurally related to a common small molecule can have a lethal effect when present as even a minor contaminant in a food supplement."[8] Lysine enhanced corn which contains high tryptophan levels, has been developed and commercialized by Monsanto and Cargill. Although this nutrition enhanced product is destined towards animal feed there is concern that transgenes might spread into corn destined for human consumption, and small amounts of tryptophan in human diets has been associated with fatalities in the late 80s.[9]

Pharming

Marvier conducted a detailed analysis[10] of pharmaceutical crop production, the regulatory mechanisms and associated dangers in California for the journal *California Agriculture* in late 2007. In California there are 18 field trial permits that have been issued thus far for the transgenic production of pharmaceutical or industrial proteins.[11] A significant battle was waged and won in 2004-2005 against Ventria Bioscience to prevent its field trials of rice genetically modified to produce synthetic human proteins. The primary concern around this particular strain of rice was the loss of rice export volumes due to cross contamination.

A variety of transgenic lettuce producing insulin developed at the University of Florida has

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recently attracted considerable media attention[12] but a review of pharmaceutical crops published at the end of 2008 sets commercial development of these crops 15 to 20 years in the future mainly due to low yields of protein recovery from such plants, "Factors affecting the yield of recombinant proteins produced in a plant system include the potential of production host and expression system, level of transgene expression and stability of the recombinant protein."[13] Even if commercialization takes place there will likely be considerable resistance to pharmaceutical crops due to concerns of cross contamination.

TABLE 1. USDA-approved field-trial permits allowing the growth of crops genetically engineered to produce pharmaceutical or industrial proteins in California, 1996–2006

Engineered crop	Applicant	Issued/ effective	Source of gene*	Pharmaceutical or industrial protein
Maize	Dow	6/2002	CBI†	CBI: Unidentified pharmaceutical protein
	Monsanto	3/2001	CBI	CBI: Unidentified transcriptional activator (pharmaceutical)
		3/2001	CBI	CBI: Unidentified transcriptional activator (pharmaceutical)
	Pioneer	3/2000	Unclear‡	CBI: Unidentified novel protein that may have pharmaceutical or industrial uses
		4/2001	Unclear	CBI: Unidentified novel protein that may have pharmaceutical or industrial uses
		4/2002	Unclear	CBI: Unidentified industrial enzyme and unidentified novel protein that may have pharmaceutical or industrial uses
		4/2004	Unclear	CBI: Unidentified novel protein that may have pharmaceutical or industrial uses
Leaf mustard	USDA Agricultural Research Service	3/2004	Unclear	CBI: Unidentified industrial enzyme
CBI		3/2004	CBI	CBI: Unidentified industrial enzyme
Rapeseed	Pioneer	9/1996	CBI	CBI: Unidentified pharmaceutical protein
Rice	Ventria Bioscience (formerly Applied Phytologics)	3/1997	Humans	Pharmaceutical proteins: Antithrombin and serum albumin
		2/1998	Humans	Pharmaceutical proteins: Antitrypsin, antithrombin and serum albumin
		2/1998	CBI	CBI: Unidentified pharmaceutical protein
		5/2000	CBI	CBI: Unidentified pharmaceutical protein and unidentified novel protein that may have pharmaceutical or industrial uses
		4/2001	Humans	Pharmaceutical proteins: Antitrypsin, lactoferrin and lysozyme
		4/2003	Humans	Pharmaceutical proteins: Lactoferrin and lysozyme
		5/2004	Humans	Pharmaceutical proteins: Lactoferrin and lysozyme
Tobacco	Planet Biotechnology	6/2006	Mice, rabbits, CBI	Antibodies to tooth decay and common cold

* Refers specifically to the gene coding for the industrial or pharmaceutical protein.
† CBI = Confidential Business Information.
‡ Source of gene coding for industrial and/or pharmaceutical protein(s) cannot be determined from publicly available information.
Source: Union of Concerned Scientists 2007.

Image 2. *Table from Michelle Marvier,* Pharmaceutical crops have a mixed outlook in California[10]

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Next Generation GE Insects

Since the late 60s scientists have speculated about stopping the spread of insect borne infectious diseases by genetically modifying the transmission vector and overwhelming the natural population through a wide-scale release. There has been special consideration and considerable emphasis on the spread of malaria and dengue fever from mosquitoes.

Perhaps one of the most crucial distinctions that has to be made between transgenic plants and the current proposals for transgenic insects is at a very fundamental level. Regardless of the sincerity or even feasibility, the rhetoric around the spread of transgenic plants, or their transgenic inserts, has been one of containment. Reassurances have been given against the spread of transgenes from plants and as mentioned previously in this report certain manipulations are being considered to engineer sterility into plants. The situation is the exact opposite when it comes to transgenic insects for the purposes of controlling disease transmission and the stated goal becomes *to spread the transgene as far and wide as possible.*

This different and alarming emphasis influences the scope of research and the options for genetic modification under consideration: although espousing to engineer reproductive sterility, the research emphasizes maximum spread and transmission of the anti-pathogen effector genes to block disease transmission.

Gene Drive Systems

Gene drive systems are the mechanistic name given to so-called "selfish genetic elements" which do not fit Mendelian inheritance ratios and spread throughout populations even if they do not confer an advantageous phenotype. Linking transgenes that inhibit disease transmission to such genetic elements is being proposed as a solution to the impracticality of overwhelming a natural population of insects with a transgenic population, especially if the anti-pathogen effector gene does not confer a strong selective advantage.[1]

A further proposition is to construct large multi-gene constructs in multiple gene drive systems that are able to spread across different vector species. Multi-gene transgenesis is being proposed in anticipation of eventual evolution of resistance to the genetic manipulation by the pathogen.[2]

There are a number of gene drive systems being considered such as transposable elements, meiotic drive genes, homing endonuclease genes and perhaps most disquietingly a naturally symbiotic microorganism of insects, *Wolbachia.*

Transposition Elements are particularly unpredictable and "frustratingly our knowledge of how transposition is regulated is still far from satisfactory."[3] Transposition events and highly mobile genetic elements have been instrumental within evolutionary processes such as horizontal gene transfer and researchers are warning us that "the wide range of hosts for Transposable Elements also brings with it a risk of movement in to non-target species."[4]

Homing Endonuclease Genes have not been observed for insect species and the current proposal is to construct an artificial HEG, a potential domain where synthetic biology might claim traction. Artificial constructs are also proposed as meiotic drive mechanisms for insects that don't have them naturally.

Wolbachia stands out amongst proposed gene drive systems as the most irresponsible consideration. In this scheme, genetically engineered *Wolbachia* microbes would be released to infect pest species, producing cytoplasmic incompatibility (CI) rendering them partially or fully sterile. This proposal is another interesting contrast to transgenic plants, where some varieties such as Bt corn are modified to prevent, not further, attack from pest organisms.

For this gene drive system, unique *Wolbachia* strains would be chosen, bred, and transformed to ensure maximum spread of infection. Transposable elements known to be active in the *Wolbachia* genome will facilitate this and possibly carry transgenes expressing a product targeting the pathogen in the vector species. *Walbachia* has been shown to facilitate Horizontal Gene Transfer[5] and contribute to the species differentiation of insects through reproductive isolation.

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The high infectivity and cross-species movement of this microbe is both its attraction and its caveat; "Its wide host range means that *Wolbachia* that are transformed to express a particular anti-pathogen product would probably also be applicable to a range of secondary vectors, although this also means there is a small risk of movement into non-target species (although such events to happen, they are ecologically very rare)."[6] Although the authors of the above paradoxical statement feel the need to doubly reassure their reader on the smallness of risk they seem to be oblivious to the basic understanding that risk is a function of both probability and consequences. The exact consequences of such an intervention are unpredictable but an uncontrollable and dangerous risk is certain.

Comments

GM Insects are not only being proposed as a way of fighting infectious diseases but also by way of similar modifications eradicating agricultural pests. A British company, Oxitech, supported by the Gates Foundation and collaborating with the USDA and University of California, Irvine amongst others, has attracted some attention as being at the forefront of GM Insect production.[7] Oxitech has been conducting field trials of GM bollworms in Arizona (where GM insect releases have been taking place since 2001) and a permit application from the USDA is pending for a 4000 acre field trial of GM bollworms in California at the time of writing.[8]

Climate Change politics will provide fertile ground for advancing this line of research. It should be expected that those engaging with commercial production of transgenic insects will claim a new mandate anticipating the rise in agricultural pests and the increased spread of insect borne diseases tied to increasing temperatures and habitats for the vectors.

Insect genetics are relatively well known due to the prevalence of the fruit fly (*Drosophila melanogaster*) as an early model species for genetic manipulation. The proposed genomic modifications (both at the level of the vector species' and their parasitic microbes) are biologically feasible and commercially applicable. Newer, gene drive systems will be presented as an improvement and ecologically sounder over older methods since less GM insects would have to be released. GM Insects produced to overwhelm naturally occurring agricultural pests (such as the cotton bollworm) will likely be equated to older techniques of releasing insects sterilized through irradiation. It will be important to evaluate the exact kind of modification to critically evaluate safety claims. As outlined above some GM insects might be engineered for increased genetic transposition while others, as proposed by Oxitech, might claim to have stabilized the transgene[9] and propose to release "millions" of "fail-safe" insects. Ultimately, the main barrier to the widespread release of GM insects will not be biological limitations but public reluctance and pressure by effective campaigning.

Transgenic Microbes

Microbes are undoubtedly the family of organisms whose genetics are most frequently modified by humans and hold the greatest population numbers and genetic diversity of all living organisms. There have been proposals for commercial applications of transgenic microbes since the 70s and others continue to be made with some recent interest in:

- Wastewater treatment by transgenic microbes for agricultural purposes[1]
- Transgenic bioremediation (an oxymoron if there ever was one): treatment of heavy metals, biofiltration of mercury, atrazine and cadmium[2]
- Transgenic microrhyzal microbes to act in concert with crop plants to mitigate drought tolerance.
- *Wolbachia* strains modified to control insect populations (see previous section)

Engineering Microbial Consortia

An interesting development in the genetic modification of microbes, which again indicates a better understanding of biology and ecological systems, is the research into what has been termed "synthetic microbial consortia." By modifying collections of transgenic colonies rather than monocultures of transgenic microbes researchers claim that they will be able to make biological circuits that can be deployed for various industrial uses, including timed releases of pharmaceuticals in animals. "Because members of microbial consortia communicate and differentiate, consortia can perform more complex tasks and can survive in more changeable environments than can uniform populations."[3] Such survivability and diversity is also relevant for the possible ecological effects since transgenic consortia would also survive and adapt more readily in natural environments. Like all GMOs "it is difficult to design either long-term homeostasis or long-term extinction into a synthetic consortium, because long-term behavior, and even the long-term genetic composition of an engineered organism, is unpredictable."[4]

Transgenic Trees

Research into transgenic trees has not been as intense as more industrialized agricultural products. A comprehensive report prepared by the Forest Society[1] details some of the considerations for transgenic traits in trees.

Similar to other transgenic plants; herbicide tolerance (especially for poplars and eucalyptus, more difficult to cultivate due to weeds), insect resistance (poplars have been transformed for defoliating insect resistance in China, the only country to have commercialized transgenic trees), disease resistance from blight pathogens, wood properties (strength and lignin content for depuplping processes and biofuel applications), abiotic stress and reproductive isolation are all avenues for transgenic investigations in trees. [2]

The conventionally accepted associated dangers from transgenic organisms are applicable to transgenic trees as well. These are adverse side effects on crop performance through plieotrophy, contamination into human food, developing pest resistance, enhanced invasiveness, harmful effects on biodiversity, genetic contamination (gene flow from trees is especially concerning since pollen from trees has a longer travel range in comparison to crops due to greater height) and horizontal gene transfer.[3]

A country by country review of transgenic tree research recently published by World Rainforst Movement (WRM) indicates that there are currently 350 outdoor test plots dedicated to transgenic trees in the US[4] mostly led by ArborGen, Oregon State University, North Caroline State University and Oak Ridge National Laboratory.[5] Of these institutions both ArborGen and Oak Ridge National Labs are conducting research to transform trees to be more applicable to biofuel production.[6] In addition, a transgenic papaya developed for resistance to the papaya ringspot virus by the University of Florida has recently completed a consultation with the FDA.

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Transgenic Vaccines

The field of vaccines poses two general areas of concern with regards to transgenesis. These areas are the political manipulation of a deeply held trust in medical justification for most technological interventions and separately the consequences and risks associated with the production and release of transgenically-produced vaccines and vaccine products. We consider these two areas separately, and briefly, below.

First, we consider the production and release of transgenically-produced vaccines and vaccine products. Products in the field of vaccines related to transgenesis are:

• Vaccines produced by microbes that have been transgenically manipulated to express viral antigens. Produced in fermentation vats, and therefore containable (at least in theory, although realistically impossible). In its most extreme form, this approach produces "Virus-Like Particles" (VLPs), which closely resemble the virus in question but is devoid of DNA/RNA and thus cannot replicate.

• Recombinant viruses. Several viral families have been transgenically manipulated to produce "chimaeric" viruses which may carry the infectivity of one with the antigenic properties of another. This strategy is most developed in the poxy-viruses, in which a bird virus may be used as a carrier of a mammal-specific one. The most active field of development is in veterinary applications, which carry medical considerations but also significant environmental consequences.

• Naked DNA "vaccines". Animals (including humans) injected with fragments of the virus in question. This creates a temporary and localized transgenesis in the animal, whose own cells express viral antigens that are then recognized by the immune system.

These products raise the following biological questions:

• Like any other genetically manipulated microbe, it is impossible to predict the behaviour of the transgenic organism if it becomes released into the environment. All other questions relating transgenics apply (e.g. antibiotic markers), but here there are a couple of additional and unique considerations. First, the possibility of horizontal gene transfer is dramatically increased in most microbial systems used in industrial production. Any escape from fermentation facilities must be understood as an escape into the larger microbial community. Accordingly, questions raised are not only limited to the ecological and physiological niche of the microbe released, but also the microbes with which such an initial release may end up exchanging genetic material. If releasing a promiscuous microbe into the environment should make us ask precautionary questions about antibiotic resistance spread, production of xenobiotic materials, nutritional and competition effects in the larger community, a microbe carrying additional viral sequences should raise yet another layer of questioning (see below). In principle, if such a microbe could be contained within the production facilities, it would raise no significant questions, but this containment is practically impossible, and releases always occur even in the best appointed facilities.

• "Mixing", i.e. recombining viruses in general should raise serious concerns. The thought is often that a chimaeric virus will not be infective and able to maintain an epidemic level because it is applied to a very distant host (e.g. avian viruses on horses). However, it is not idle to consider that the virus will likely not remain in the intended host, in effect causing an environmental release. In the case of avian pox viruses, there is usually no consideration for example of the obvious question of infectivity in wild birds, and what consequences an epizootic may have at an environmental and ecological levels.

• Naked DNA virus treatments raise quite unique questions. Because they are currently applied mostly in fish (although there are suggestions that they should also be applied on humans in Africa), there has been precious little discussion of these questions. We point out here only as markers of concern the fact that a transient, localized transgenesis of the host (the "vaccine" recipient) should raise serious medical as well as ethical questions. A good treatment of some of these questions was produced already a decade ago by a Norwegian study[1], yet the questions raised by this unique study are still open and unanswered. More recent studies indicate that the "transient" temporality of the manipulation may not be so negligible, since DNA introduced into fish was found to be inserted into the fish genome for the life of the fish.

With regards to political considerations, the "medical exemption" argument raised by promoters of biotechnology is very strongly bolstered by the vaccine applications of transgenesis discussed above. It is true that many applications in each category considered in the vaccination field actually work in inducing active immune response and therefore protection of the recipient. This effectiveness is held as a reason to preempt any discussion of concern or precaution. In its coarsest form, such an argument suggests that considering precautionary questions can prevent the growth of a desired industry and its concurrent jobs, economic development, etc. It must be noted that such arguments have been proven effective in real situations, most directly in the campaign to defeat Measure M in Sonoma County.

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California Specialty Crops

A review of field test permit applications[1] was conducted for the agricultural products identified as California's specialty crops by the California Specialty Crops Council.[2] This review also identified that research into and general promotion of genetic engineering for most of these crops was waning, most likely due to public skepticism of the transgenic manipulations.

The majority of transgenic research is likely to stay in the realm of industrially produced agriculture but there will continue to be proposals for transgenesis in minor crops.

Avocado- No field trial applications since 2003.

Apple- A field trial permit was granted to UC Davis in September 2008. Research is being done into suppressing ethylene, a compound that mediates ripening processes. There is further research done by Cornell University.

Dry Bean- Field trial permits have been issued to Michigan State University for herbicide tolerance and fungus resistance research.

Carrot – Research appears to be stagnant, no new field trial permits issued since 2001.

Plum – Research being done by Clemson University and the USDA. Field Trial permits issued for trangenes associated with ripening and pesticides against root diseases such as Root Knot Nematode and Phytophthora Root Rot. APHIS has deregulated USDA's Plum Pox Virus resistant transgenic plum[3] and the FDA has recently completed a consultation.[4]

Melon – Permit issued to Texas A&M for transgenes delaying fruit ripening.

Garlic- No field trial permit applications.

Onion – Monsanto and its subsidiary Seminis Vegetable Seeds are developing glyphosate tolerant onion and permits have recently been taken out. Onion is an attractive plant for Roundup Ready product development since weed management during onion cultivations is especially taxing because of relatively slow growth and lack of a sufficient leaf canopy that would suppress weed growth. A glyphosate resistant onion might have market attraction.[5]

Peach- No field trial permit applications.

Pears – Research seems to be stagnant, no new field trial permits issued since 2001.

Peppers - Research seems to be stagnant, no new field trial permits issued since 2000.

Grapes – June 2008 permit issued for a California field trial to Cornell University for a transgene for virus resistance.

Floriculture

A joint venture between Mendel Biotechnology from Hayward, California and a German plant breeding company, Selecta Klemm, called Ornamental Biosciences has been attempting to engineer drought tolerance into ornamental products to market worldwide. According to Mendel Biotechnology vice president James Zhang, these ornamental products will be attractive to consumers worried about water consumption in the coming climate age of austerity measures as well as providing the convenience that "people don't have to worry about plants dying if they forget to water them or while [they are] on vacation."[6] Fungal resistance is another Ornamental Biosciences project they present as "ecological genetic support" since it is claimed that it will reduce pesticide use although the failure of glypohosate, marketed similarly, is acknowledged far and wide.[7]

There are also manipultion plans for pigment genes in order to produce naturally absent colors in some flowers. An Australia-based company Florigene has been selling transgenic blue carnations for ten years in 3 countries and is currently working on blue roses and has a pending petition for deregulation.[8] The floriculture market is significantly smaller than industrial agriculture and less R&D resources are available therefore significant movement in this field in the near future is unlikely.[9]

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Ecosystem of California Biotech

"A new ecosystem of companies will be generated by the EBI deal"

Prof. Dan Kammen, one of the names behind the Energy Biosciences Institute (EBI) comprised of UC Berkeley, the University of Illinois – Urbana Champlain and British Petroleum[1]

On February 1, 2007, California became home to the most extravagant and expensive partnership between a public university and a corporate entity. BP (formerly known as British Petroleum but using the misnomer Beyond Petroleum) announced[2] it would be bankrolling the $500 million Energy Biosciences Institute and was poised to reap most of its rewards. These rewards will both arise from research (in terms of monopolies over results and in giving overall direction) but also from the cleansing effect an association with a public university to investigate "renewable energy" has for a primarily fossil fuel company blamed for climate changes. The Energy Biosciences Institute has been thoroughly critiqued in relation to academic freedom, the corporatization of public universities and the potential environmental and social consequences of the proposed research.[3]

The assertion by Prof. Dan Kammen, points to a preexisting condition of California and the Bay Area in particular, of being at the forefront of the commercial development and deployment of biotechnology products. Early biotech pioneers such as Genentech (the first biotech company), Advanced Genetic Science (the first environmental release of a GMO, the ice-minus bacteria) and Calgene (the production of the fist commercialized transgenic agricultural product, the Flavr Savr tomato) have all originated in California.

As a biotechnology stronghold California has been at the very forefront of conjoining concerns around Climate Change with aspirations of profit making. Major California research institutes such as the Energy Biosciences Institute (EBI), the Joint Bioenergy Institute (JBEI) and biotechnology companies such as Mendel Biotech, Amryis, LS9 and Ceres, Inc. are all deeply involved in genetically transforming organisms for biofuels.

The constellation of prestigious public research universities, venture capital and major agricultural production has made California the center of agricultural biotechnology development. According to the University of California, California is "Home to one-third of the nation's biotechnology firms. California has more biotech jobs than all of the other states combined. One in four U.S. biotech companies is located within 35 miles of a UC campus. One in three California biotech firms (and one in six nationwide) was founded by UC scientists, and 85% of California biotech firms employ UC alumni with graduate degrees."[4]

For those in California who want to effectively counter the commercialization of transgenic technologies, targeting the sites of its development might provide an attractive target.

It is near impossible to cover the entire gamut of California biotech working on issues associated with climate change but below we present some of the key players and look at some of the research areas pursued by them.

EBI: The Energy Biosciences Institute is in the process of constructing its major facility, the Helios Building, in Berkeley CA but is already operational in facilities spread around the UC Berkeley and University of Illinios, Urbana-Camplain campuses. Amongst some of the research conducted at the EBI are engineering *Mischantus* for maximum yield, microbes for enzyme production (hemicellulases and cellulases) to be used in cellulosic biofuels production, bacteria for biodeisel production, yeast for more efficient sugar fermentation and microbes for microbially enhanced hydrocarbon recovery (MEHR) from fossil fuels.[5]

JBEI: The US Department of Energy, $125 million, Joint Bioenergy Institute is located in Emeryville, CA and is comprised of three national laboratories (Lawrence Berkeley National Laboratory, Sandia National Laboratories, and Lawrence Livermore National Laboratory), two universities (UC Berkeley and UC Davis) and a foundation (Carnegie Institute for Science, Stanford). JBEI is engaging in feedstock development, lignocellulose deconstruction and engineering

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microbes to convert sugars and other aromatic compounds into biofuels.[6]

While it might appear as a public initiative, "JBEI is positioned to take advantage of the significant capabilities of its partners and other institutions and companies in the San Francsico Bay Area. JBEI's close working relationship with its industry partners will ensure that JBEI creates the fundamental knowledge and scalable technologies to solve real-world problems in commercial-scale biofuels production."[7]

Amyris: Also located in Emeryville, CA, Amryis is the start-up synthetic biotech venture of Jay Keasling, a UC Berkeley Professor with appointments at EBI and JBEI. With a pilot plant in California and another planned for Brazil, Amyris is conducting research into engineering microbes and enzymatic pathways for new biofuels. Amyris has recently registered a biodiesel fuel with the EPA.[8]

LS9: Located in South San Francisco, LS9 is another synthetic biology company working on engineering microbes to process feedstock into fuel that would be compatible with existing petroleum infrastructure. One of its founders Chris Somerville currently heads the Energy Biosciences Institute.[9]

Mendel Biotech: Mendel Biotechnologies is located in Hayward, CA. Chris Somerville from LS9 and the EBI was the previous CEO of Mendel Biotechnologies and currently resides on the board and UC Berkeley professor Brian Staskawicz is also part of this company. Mendel conducts extensive research into engineering crops for yield increases and abiotic stress tolerance. In 2005 Mendel formed a partnership with British Petroleum to develop feedstocks for biofuels[10]

Aurora Biofuels: Located in Hayward, CA, Aurora Biofuels concentrates on producing biofuels from algae, has had a pilot plant in operation since 2007 and claims to be able to open a commercial scale plant in 2012. Aurora's newly appointed CEO Robert Walsh used to be the president of LS9 after a 26-year career at Royal Dutch Shell. Dr. Krishna Niyogi a UC Berkeley professor of Plant and Microbial Biology resides on its scientific advisory board.[11]

Ceres, Inc.: With it's headquarters in Thousand Oaks, CA, Ceres Inc., claims to hold "the world's largest collection of plant gene intellectual property."[12] Ceres is primarily involved in producing engineered feedstock crops and "projects that average productivity of cellulosic energy crops of 15 tons per acre (roughly three times current productivity for switchgrass) can be achieved across a broad range of geographic and climate regions – including most of the continental United States – in ten years, given an aggressive effort using modern breeding techniques."[13] Ceres' Chief Scientific Officer Richard Flavell is a UCLA professor.[14]

Arcadia Biosciences: Arcadia, located in Davis, CA announced in January 2008 that it had completed a successful field trial of tobacco engineered for drought tolerance and has been engineering crops such as canola, tobacco, cotton, tomato and rice for abiotic stress tolerance and nitrogen uptake efficiency.[15]

The short profiles on the above companies provide insight into the revolving door between public universities and private biotechnology ventures. This meshing and conflicting of interests' raises serious questions in terms of the direction of research meant to be conducted in the name of the public good. Pioneering institutions of the California biotechnology ecosystem are not only instrumental in producing the research that leads to transgenic products in California but all around the world and should be combatively opposed.

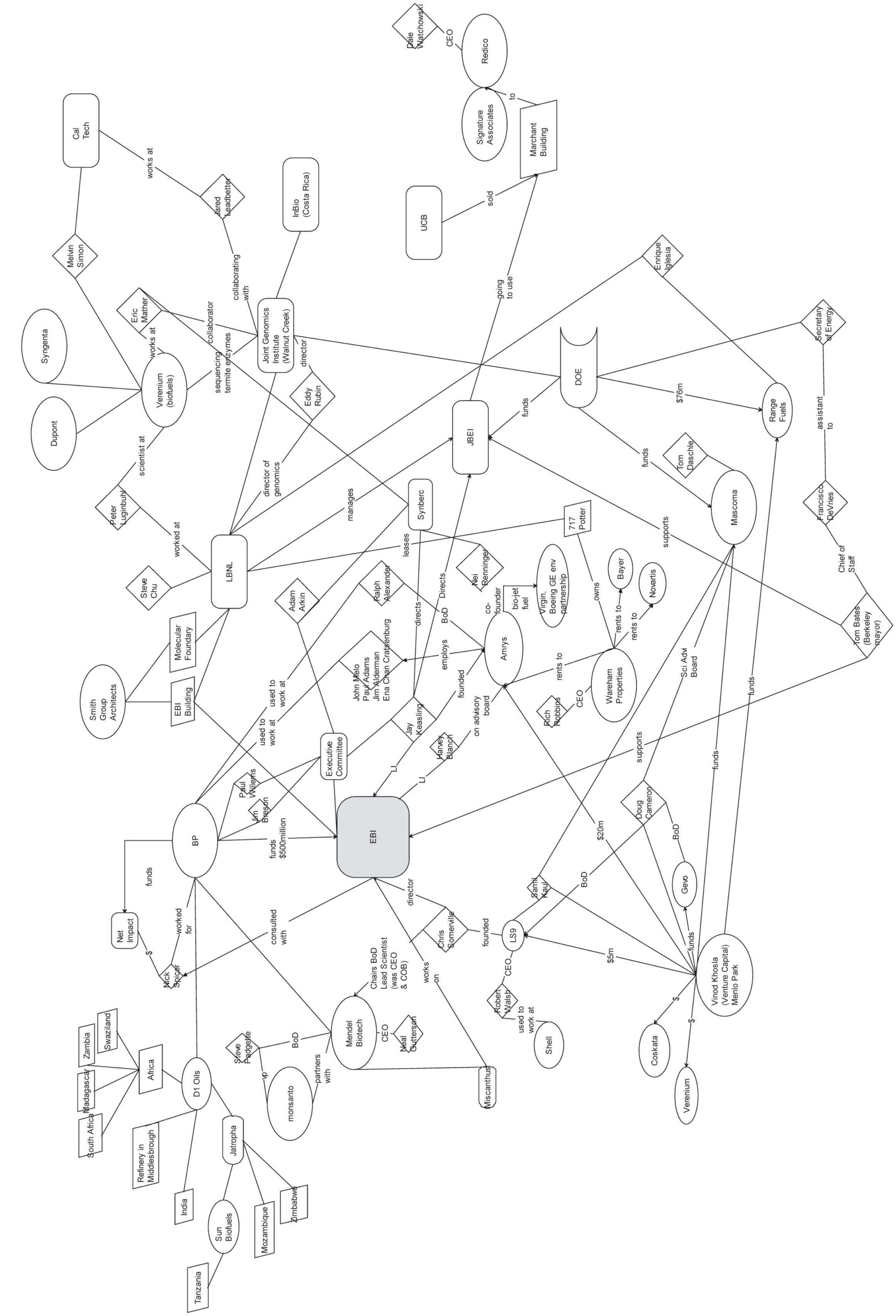

Image 3. *Initial Mapping of the Energy Bioscience Network Centered around the EBI by Aaron deGrassi (2007)*

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