

## Forest biotechnology advances to support global bioeconomy

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**Abstract** - The world is shifting to an innovation economy and forest biotechnology can play a major role in the bio-economy by providing farmers, producers, and consumers with tools that can better advance this transition. First-generation or conventional biofuels are primarily produced from food crops and are therefore limited in their ability to meet challenges for petroleum-product substitution and climate change mitigation, and to overcome the food-versus-fuel dilemma. In the longer term, forest lignocellulosic biomass will provide a unique renewable resource for large-scale production of bioenergy, biofuels and bio-products. These second-generation or advanced biofuels and bio-products have also the potential to avoid many of the issues facing the first-generation biofuels, particularly the competition concerning land and water used for food production. To expand the range of natural biological resources the rapidly evolving tools of biotechnology can ameliorate the conversion process, lower the conversion costs and also enhance target yield of forest biomass feedstock and the product of interest. Therefore, linking forest biotechnology with industrial biotechnology presents a promising approach to convert woody lignocellulosic biomass into biofuels and bio-products. Major advances and applications of forest biotechnology that are being achieved to competitively position forest biomass feedstocks with corn and other food crops are outlined. Finally, recommendations for future work are discussed.

**Keywords** - Forest biotechnology, bio-economy, biofuels, bio-materials

### Introduction

Bioeconomy encompasses all economic activities that are fueled by research and innovation in the biological sciences. It is a large and rapidly growing segment of the global economy that provides significant public benefit (OECD 2009). Also, it has emerged as a worldwide priority because of its tremendous potential for growth and the numerous societal and environmental benefits it offers. Bioeconomy can help to reduce the world dependence on fossil fuels, address key environmental challenges, transform manufacturing processes, and increase the productivity and scope of the agricultural and silvicultural sectors while creating new jobs and innovative industries.

Food, feed, energy, and industrial products demand will increase concomitantly with human population and climate change. This production therefore needs to be high enough and, at the same time, minimize or prevent harm to the environment. Yet, this balance cannot be achieved with current strategies. Moreover, food and energy crises have often occurred in the past. In recent years, the rapidly increasing demand for food (i.e., for human populations and livestock) along with biofuels has led to food price volatility (Battisti et al. 2009).

Based on recent findings, new avenues for forest breeding which take into account the integration

of modern genetic and genomic techniques with conventional breeding will expedite forest tree improvement (Harfouche et al. 2012a and 2014). In this context, we argue that forest breeders and land owners have the opportunity to make use of modern biotechnologies in an innovative ecologically sound silviculture.

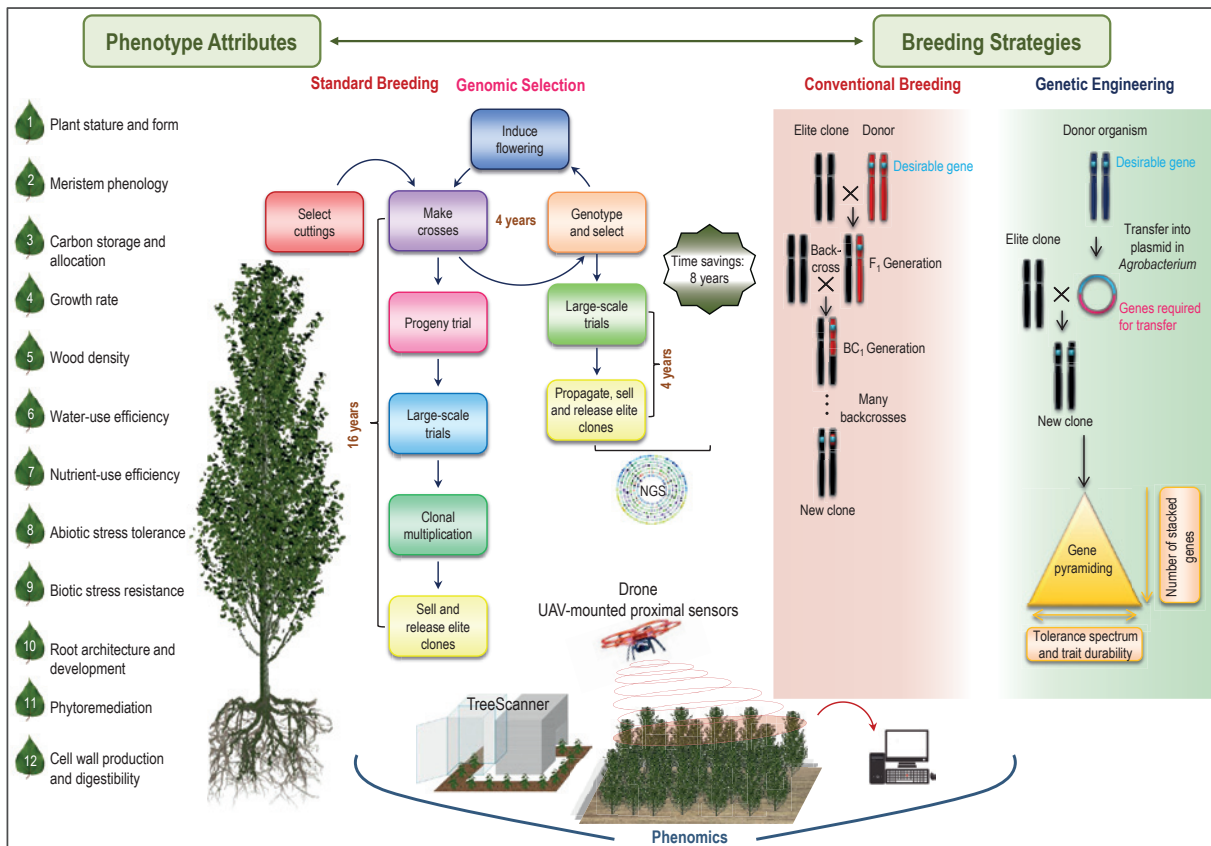
In addition, as we are advancing towards a global economy that is attempting to find ways to break its addiction to fossil fuels and develop an economy based on renewable biological materials and energy sources, forest biomass is being actively explored as a possible substitute in many parts of the world.

Forest trees constitute about 82% of the continental biomass (Roy et al. 2001) and harbor more than 50% of the terrestrial biodiversity (Neale and Kremer 2011). They also help to mitigate climate change, and provide a wide range of products that meet human needs, including wood, biomass, paper, fuel, and bio-materials (Harfouche et al. 2012a). However, forest trees grown in the field are usually exposed to environmental stress. Current and predicted climatic conditions, such as prolonged drought, increased soil and water salinity, and low-temperature episodes pose a serious danger to forest productivity, affecting tree growth and survival (Harfouche et al. 2014).

Conventional breeding has been successful at ameliorating several phenotypic characteristics that

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**Figure 1** - A schematic representation of integrated forest breeding strategies in next generation genomics and phenomics era focusing on poplar as the tree model species for biofuel research. Incorporation of Next-Generation Sequencing (NGS) based multi-omics approaches with genetic engineering, Genomic Selection and phenomics can be used to speed up tree breeding and save time as compared with conventional breeding. These new varieties will maximize yield per acre with minimum inputs and exhibit value-added traits that enhance their use as biofuel and bio-based feedstocks.

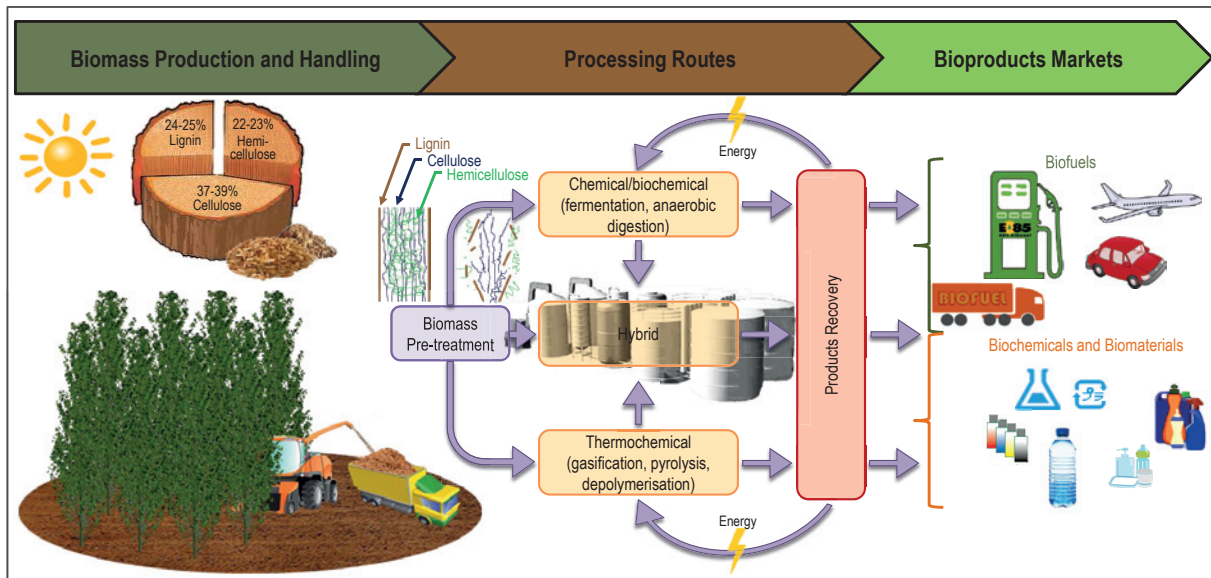
impact tree growth, such as crown architecture and partial resistance to biotic stress. But, continued improvement of forest trees by traditional means is slow due to their long generation times and large genomes (Neale and Kremer 2011). Nevertheless, over the past two decades, genetic improvement opportunities have been broadened by genetic engineering targeting important traits in model forest-tree species (Harfouche et al. 2011). This stems from the urgent need to better understand how forest trees adapt to severe environmental conditions in order to develop new and improved varieties that are able to sustain productivity and meet future demands for commercial products. For example, the completion of a draft genome sequence of the poplar (*Populus trichocarpa* Torr. & Gray ex Brayshaw; Tuskan et al. 2006) has advanced forest tree genetics to unprecedented levels. Recent releases of the genome sequences of white spruce (*Picea glauca* (Moench) Voss; Birol et al. 2013), Norway spruce (*P. abies* L.; Nystedt et al. 2013) and Eucalyptus (*Eucalyptus grandis*; Myburg et al. 2014) and the anticipated release of the Pinus genome will undoubtedly lead to more rapid advances.

Despite the enormous promise of advanced forest biotechnology, it has yet to gain traction as a viable breeding alternative, mainly because of its

exhaustive biosafety regulations and the divided public opinion over it. Besides, understanding the relationship between genotype and phenotype and dissecting complex polygenic traits in forest trees becomes a central goal in tree genetic improvement.

In addition, innovative technologies, such as genomic selection (GS) and next-generation Eco-tilling (Harfouche et al. 2012a), are now proving to be important strategic approaches to improving our understanding of various processes in forest trees and the role of key genes associated with their regulation (Resende et al. 2012, Vanholme et al. 2013). Although there have been considerable advances in our understanding of lignin biosynthesis and monomer composition, most of the genetic engineering efforts have been restricted to poplars, and overcoming biomass recalcitrance due to novel engineering of lignin pathways in other forest trees is still in its infancy.

This article provides a summary of recent achievements in forest biotechnology with an overview on the integrative approach to accelerate the development of improved forest feedstocks for a sustainable bioeconomy (Fig. 1). Furthermore, it discusses new approaches and concepts (Fig. 2, 3 and 4) to advance the forest-based bio-economy and issues that should be considered when devel-



**Figure 2** - The integrated biorefinery concept. Forest lignocellulosic biomass are ideal feedstocks that can be used to produce bioenergy, biofuels and bio-products, using thermochemical or biochemical conversion routes, or a combination of both.

oping and deploying biotech trees with improved attributes.

### The emerging global bioeconomy

Bioeconomy involves the sustainable production of renewable biological resources and their conversion into food, feed, biofuels, bioenergy, and bio-products by harnessing the power of biotechnology, but at the same time preserving the environment and ecosystem services. In this article, bio-based production encompasses items produced from forest biomass feedstocks including biofuels, bioenergy and bio-products or bio-materials (largely bio-chemicals and bio-plastics) (Fig. 2).

Until recently, in most countries the focus has been to a great extent on first-generation biofuels production. However, second-generation biofuels and bio-materials offer exciting opportunities for future manufacturing to replace existing fossil-based materials with bio-based, therefore, contributing to greenhouse gas (GHG) emissions reductions. Yet, green credentials are not enough to justify their place in the market. Therefore, the technical, economic and social performances of these materials have to be considered (Philp and Pavanan 2013). In addition, bio-based production promises high-value jobs. Carus et al. (2011) have estimated that materials use of biomass can directly support 5-10 times more employment and 4-9 times the value-added compared with energy uses, principally due to longer, more complex supply chains for material use. Moreover, a report commissioned for The Blue Green Alliance estimated that shifting 20% of current plastics production into bio-plastics would create

a net 104,000 jobs in the US economy (Heintz and Pollin 2011).

However, if a bioeconomy is to succeed in any country, it should rely on international cooperation and trade (Philp and Pavanan 2013). On the one hand, the drivers behind the development of bio-based production are global: climate change mitigation, energy security and independence, the attraction and creation of new jobs associated to rural regeneration. On the other hand, global food security is a grand challenge facing society, and there are ways in which energy and food production come into direct competition (Seidenberger et al. 2008).

Bioeconomy is becoming a reality in many parts of the world as it offers great opportunities and solutions to tackle major societal, environmental and economic challenges. A global bio-economy that is also based on agricultural and forest biomass is emerging in Europe, the United States and Canada that offers an avenue toward a more low-carbon green economy. Exploitation of non-food feedstocks such as forest biomass is gaining importance for this sustainable production.

The bioeconomy concept is currently flexible and it is interpreted differently in different countries and regions. While, many countries have already published national strategies and visions on the bioeconomy (i.e., The Bio-economy to 2030: Designing a Policy Agenda by OECD, the National Bio-economy Blueprint in the United States, Innovating for Sustainable Growth: A Bio-economy for Europe, The Canadian Blueprint: Beyond Moose and Mountains) some have established organizations and networks to stimulate and develop it. Though, sustainability

is recognized as important, the driving force behind the bioeconomy is the opportunity for economic growth and innovation.

### The role of forest biotechnology in a sustainable bioeconomy future

The tools of biotechnology have the potential to produce a new generation of genetically improved bioenergy crops that are engineered to either produce high biomass yield and digestibility, or offer protection to bioenergy crops against environmental stresses, or a combination of all attributes (Fig. 1).

Lignocellulosic biofuels promise to resolve the most significant problems associated with existing first-generation biofuels. For example, Littlewood et al. (2014) have recently shown that bioethanol from poplar biomass feedstock is a commercially viable alternative to fossil fuel in the European Union. A techno-economic modeling to compare the price of bioethanol produced from short rotation coppice (SRC) poplar feedstocks under two leading processing technologies (dilute acid and liquid hot water), in five European countries (Sweden, France, Italy, Slovakia, and Spain) has been used. In a forward-looking scenario, genetically engineering poplar with a reduced lignin content showed potential to enhance the competitiveness of bioethanol with conventional fuel by reducing overall costs by approximately 41% in four out of the five countries modeled (Littlewood et al. 2014). Current research and development (R&D) also focus on evaluating poplar biomass production potential in a SRC. Such research is critical for investigating the performance of novel poplar genotypes deriving from standard breeding programs with potential for commercial biomass production over multiple coppice rotations. Results by Sabatti et al. (2014) showed that poplar biomass production differed significantly among rotations starting from 16 tons/ha/year in the first, peaking at 20 tons/ha/year in the second, and decreasing to 17 tons/ha/year in the third rotation. This will ultimately lead to a more efficient economic feasibility of utilizing tree woody biomass for biofuels and bio-materials.

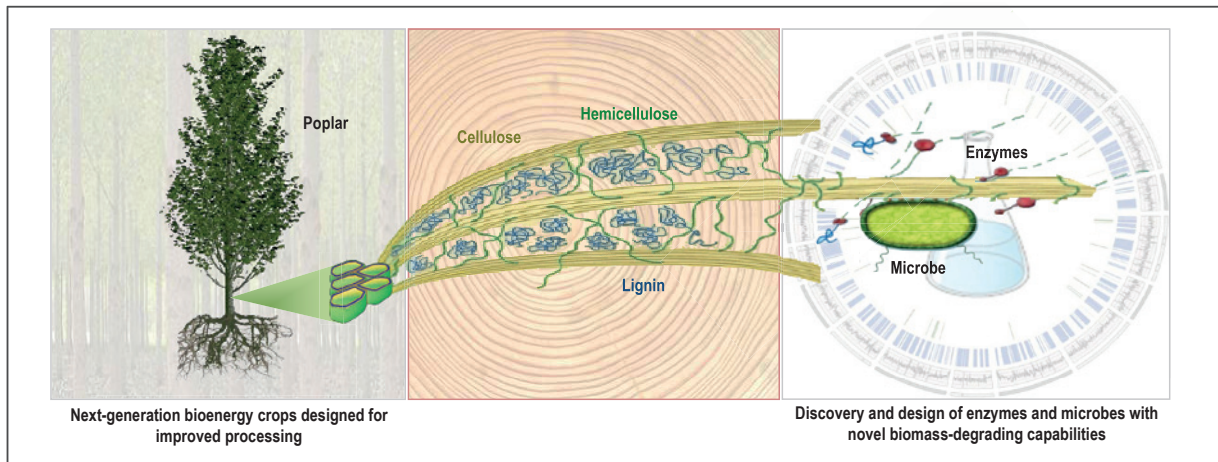
Miscanthus can greatly reduce the land intensity of biofuel production. While only 4.5 dry tons of harvestable corn grain are extracted from each acre of corn grain, 13 dry tons of harvestable biomass of Miscanthus is produced per acre. Thirteen-hundred gallons of cellulosic ethanol can be produced per acre of Miscanthus biomass plantation. Only 450 gallons of corn-ethanol are yielded per acre of corn. In the United States, a hypothetical scenario to produce 35 billion gallons of bioethanol, using corn as a feedstock would demand one-quarter of

all harvested cropland. However, using Miscanthus bioenergy crops would need less than one-tenth (Heaton et al. 2008).

Biotechnologically-improved bioenergy crops such as poplar can also be grown on marginal and drought-prone lands where major crops are less productive. This would permit to ease the competition on land and water resources to be used for food and feed. Recently, it has been shown that the constitutive overexpression of the wintersweet (*Chimonanthus praecox*) fatty acyl-acyl carrier protein thioesterase (CpFATB) in poplar activates an oxidative signal cascade and leads to drought tolerance in the transgenic plants. The genetically engineered poplar maintained significantly higher photosynthetic rates, suggesting that changes in fatty-acid composition and saturation levels may be involved in leaf tolerance to dehydration during drought stress (Zhang et al. 2013). Another important study reported that gene stacking by overexpressing multiple resistance genes enhanced tolerance to environmental stresses in transgenic poplar. The transgenic lines harboring effector genes: *vgb*, encoding aerobic *Vitreoscilla hemoglobin*; *SacB*, encoding a levansucrase that is involved in fructan biosynthesis in *Bacillus subtilis*; and *JERF36*, a tomato gene encoding jasmonate/ethylene-responsive factor protein exhibited higher growth than the controls, as demonstrated by greater height, basal diameter, and biomass than the corresponding non-transgenics. This improved growth could be primarily due to higher water-use efficiency and fructan levels, and better root architecture under drought and salinity stress (Su et al. 2011).

These selected recent advances in maximizing tree tolerance to drought stress will allow an important bioenergy crop to be bred so it will grow in less than ideal soils and climate. Together, these results demonstrate the potential of forest biotechnology for improving environmental stress tolerance and biomass processability in forest trees.

Equally important, GS is extremely appealing in forest trees due to the prospects of improving accuracy when selecting for traits with low heritability (e.g., biomass productivity and abiotic stress tolerance) and where long generation times and late-expressing, complex traits are involved (Gratapaglia and Resende 2010). However, successful application of GS in tree breeding programs aimed at developing trees that are tolerant to environmental stresses or to dissect quantitative trait variation will require comprehensive physiological information that rely on rigorous phenotyping. Therefore, high-throughput phenotyping of morpho-physiological traits will require the utilization of sophisticated, non-destructive imaging techniques in a multi-



**Figure 3** - An integrated multidisciplinary approach linking forest and industrial biotechnology to overcome the recalcitrance of biomass toward processing.

spectral approach. For example, near-infrared spectroscopy, canopy spectral reflectance, and infrared thermography can be used to assess biomass productivity and plant water status, and to detect environmental stresses at the individual-tree level. These sensors can be mounted on drones, which can be directed with a global positioning system to enhance the precision and accuracy of phenotyping under field conditions (Harfouche et al. 2014).

This phenomics approach further creates opportunities to overcome the field-based phenotyping bottleneck and generate phenotyping sets, such as environmental stress tolerance and biomass estimation. Ultimately, it will help to uncover phenotype-to-genotype relationships and their relevance for improving tolerance to environmental stresses in forest trees (Fig. 1). GS coupled with phenomics offers great promise for forest breeders in accelerating the genetic improvement of forest trees as bioenergy feedstocks.

Biotechnology has the potential to not only produce more productive bioenergy crops and minimize inputs, but also to develop more efficient biofuels and bio-materials conversion processes. This offers a great cause for optimism that the global bioeconomy challenges of the new century can be met.

### **Linking forest and industrial biotechnology to accelerate drive towards sustainable bioeconomy**

Undoubtedly, one of the greatest impediments to commercializing second-generation biofuels along with bio-materials that has yet to be solved is that most of the conversion processes are not yet ripe, costly and time-consuming. An integrated second-generation biorefinery can use either a biochemical or thermochemical process, or a hybrid of both, in order to process efficiently biomass feedstocks into multi-purpose products with great added-value (Fig.

2). The biomass-tailored thermochemical conversion system relies on heating the feedstock to high temperatures with little or no oxygen. Whereas, the biochemical system relies on the use of microorganisms and enzymes to process the biomass and on the genetic engineering of these microorganisms for more efficient biological conversion. The concept of coupling green (plant) and white (industrial) biotechnology is proposed here (Fig. 3). R&D focusing on the synergistic interaction between these two biotechnologies are therefore of paramount importance. Plant biotechnology is, on one hand, playing an important role in the development of advanced biomass feedstocks for a bioenergy and bio-products industry. On another hand, industrial biotechnology is involved in the conversion of these renewable and sustainable resources into a wide range of biofuels and bio-materials (Fig. 2 and 3).

Lignocellulosic biomass are mostly composed of cellulose, hemicellulose, and lignin, which serve to maintain the structural integrity of plant cells (Fig. 2 and 3). Lignocellulosic woody materials have great potential for biofuel and bio-materials production. The plant cell wall polysaccharides can be used as a feedstock for biofuel production after being broken down into simple sugars (saccharification) (Ragauskas et al. 2006, Solomon et al. 2007), but lignin strongly impedes this process (Boerjan et al. 2003). A highly degradation-resistant phenolic polymer, lignin is part of a complex matrix in which cellulose microfibrils are embedded. The inhibition of saccharification enzymes by lignin may result from the reduced accessibility of cellulose microfibrils, as well as the adsorption of hydrolytic enzymes to the lignin polymer (Weng et al. 2008). Furthermore, current chemical and physical strategies to remove lignin from biomass, such as pretreatment with steam or acid, result in the formation of compounds which can inhibit downstream processes of saccharification and fermentation (Hamelinck et al.

2005). All together, these lignin properties are hard to deal with and make its biosynthesis a key control point in biomass degradation and in determining the efficiency of biofuels production (Weng et al. 2008).

In addition to work being conducted *in planta* using genetic engineering, with the goal of manipulating lignin content and monomer composition, another line of experimentation is to discover novel strategies for lignin degradation. Therefore, R&D aimed at increasing the efficiency and decreasing cost of lignocellulosic biomass pretreatment is currently a high priority along with the metagenomic discovery of biomass-degrading genes and genomes. For example, recent deep sequencing data sets in the cow rumen microbes provided a substantially expanded catalog of genes and genomes participating in the deconstruction of cellulosic biomass (Hess et al. 2011). In addition, recent release of the genome sequence of white rot fungus (*Phanerochaete chrysosporium*) has shown that the genome of this fungus encodes hundreds of enzymes potentially dedicated to lignin degradation (Martinez et al. 2004, Vanden Wymelenberg et al. 2006). Thus, harnessing this rich biological diversity that has recently started with the metagenome sequencing of the gut flora of *Nasutitermes* is an important step forward for lignin degradation (Warnecke et al. 2007). Likewise, a deeper understanding of termite lignocellulose digestion by metagenomics could shed light on the enzymatic mechanisms useful for biomass delignification.

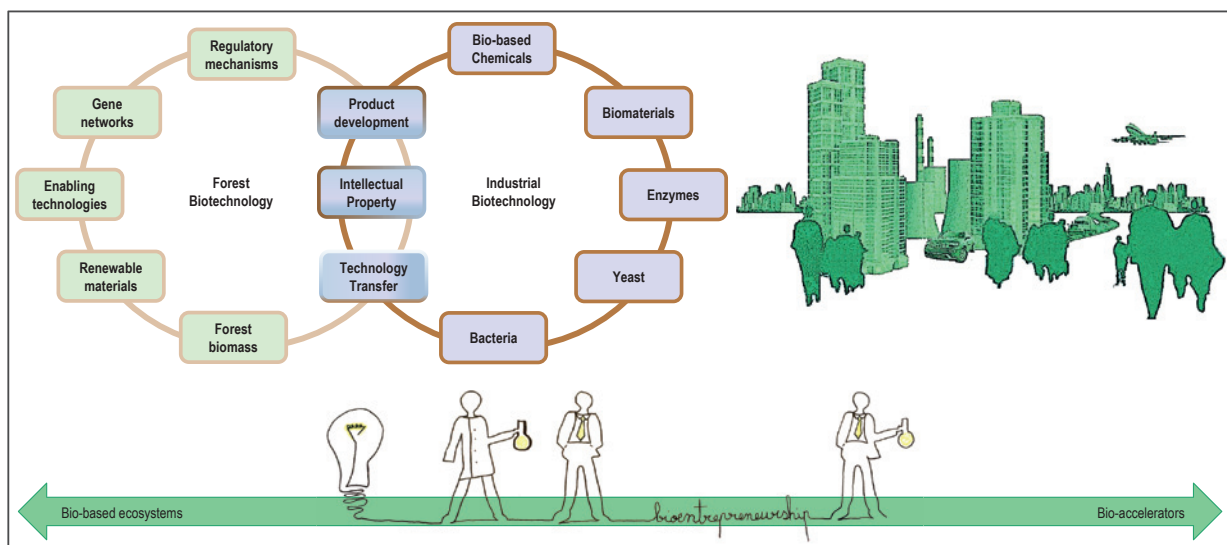
### Building skills for Europe's bioeconomy: the role of biotechnology and entrepreneurship

Bioeconomy is one of the world's most educated

industries. These creative scientific minds drive the global bioeconomy where Small and Medium Size Enterprises (SMEs) constitute ~80% of the companies in most developed countries' bio-economy. Besides, the bio-economy in Europe is currently worth more than € 2 trillion a year and employs over 22 million people, predominantly in rural areas and often in SMEs (Ernst & Young 2012).

Entrepreneurship education is now recognized as an important part of fostering entrepreneurial activity in the European Union. Entrepreneurship in biotechnology has a great potential to maximize the impact and commercial potential of the bio-economy (Fig. 4). The significant growth of the biotechnology sector over the last decade means that biotechnology enterprises are seen as playing a vital role in creating solutions and jobs in the future. For example, Harfouche et al. (2010) have recently shed light on how to protect biotech-based innovation for the development of feedstock for second-generation biofuels and strategies for technology transfer to show the important role biotechnology Intellectual Property plays in the global bioeconomy (Harfouche et al. 2012b).

Important prerequisites for a competitive bio-economy is the availability of well-trained workforce with the necessary entrepreneurial mindset and business skillsets. To move this forward, European efforts have recently sought to develop new learning and teaching model for entrepreneurship education in biotechnology to train the next-generation of talents to turn vision into reality. A two-year Knowledge Alliance project funded by the European Commission which brings together a knowledge and innovation community through partnership across Europe ([www.bioinno.eu](http://www.bioinno.eu)) for biotechnology



**Figure 4 -** Building skills for Europe's bio-economy. An increased focus on entrepreneurship, translational sciences, regulatory science, product development, and technology transfer in biotechnology and forestry can help accelerate movement of bioinventions out of laboratories and into markets.

entrepreneurship education has recently initiated. This program will focus on teaching biotechnology entrepreneurship with an emphasis on innovative biotechnology applications in agriculture, forestry, and bio-based economy.

With innovations in biotechnology at the core of the success of global bio-economy, and the world's need for a more accessible and translational science, this challenge will have to be tackled by governments and industry associations. Greater investment in R&D and integration of bio-entrepreneurship education and traineeship are also necessary to react to global bioeconomy challenges.

### What next?

Future R&D directions and key actions that need to be taken to tackle the managerial, economic and political challenges facing the forest-based bio-economy are highlighted.

- (i) We need to adopt an all-inclusive approach among forest biomass developers, land-owners, biofuels producers, end users and policymakers. This will enhance our ability to develop bioenergy crops for the growing bio-economy agenda. Government interventions with subsidies for production, consumption and R&D are instrumental in the promotion of second-generation biofuels.
- (ii) With unprecedented recent technological advances in the areas of genomics and phenomics, we are now well poised to capitalize on these strategies to speed up the development of ideal forest biomass feedstocks for bio-economy. Ultimately, this holistic approach will deepen our understanding of forest tree breeding and enhance our ability to develop desired tree phenotypes.
- (iii) Water supply is obviously another crucial factor in sustainability of forest biomass production. The scale of its importance is worth highlighting. As it is often necessary to grow forest trees on marginal land, where water and nutrient resources are limiting, it will become increasingly important to improve water and nutrient use efficiency in forest trees using biotechnology to ensure sufficiency and sustainability. To reap these research-proven benefits, biosafety regulations must be improved and public acceptance must be properly addressed.
- (iv) Another major obstacle to industrial-scale biofuels production from lignocellulosic biomass lies in the inefficient deconstruction of plant cell wall material. Metagenomics aimed at retrieving novel enzymes from naturally

evolved biomass-degrading microbial communities coupled with in planta engineering should aid in the optimization of biofuel and bio-materials production and the development of advanced bioenergy crops.

- (v) High octane fuel blends have a great potential to expand the market for advanced second-generation biofuels, increase engine efficiency, and reduce GHG emissions from transportation sector. Before these benefits can be realized, key market and regulatory challenges must be overcome.

With growing global commitments to energy security and climate change mitigation, the world have a great opportunity to reap the benefits of economic growth, jobs creation, and environmental improvements that bio-economy plans promise. We hope these endeavors will encourage greater international coordination and cooperation from both public and private sectors for R&D.

### Concluding remarks

The world's ambitious plan to reduce its carbon footprint has led to the emergence of a new bio-economy, one in which non-food forest-based biofuels and bio-products have a significant advantage over fuels and products that are non-renewable and require large amounts of fossil fuel energy to manufacture. Yet, this will require more forest biomass resources and a rigorous forest management, in order to be well positioned to ensure sufficiency and sustainability in the production of new bio-products while creating new jobs and preserving the ecosystem services (e.g., water-quality protection, as well as wildlife conservation).

By producing biofuels and bio-based materials from wood, forest products companies can capture new markets, and support rural communities and government services.

There are numerous viable strategies to convert forest biomass into biofuels and bio-materials. Yet, to maximize jobs and economic returns, these strategies have to be integrated with the existing forest products industry.

In this article, we propose to integrate novel genetics, genomics and phenomics with conventional breeding to expedite forest tree improvement. This integrative approach could prove a useful tool for speeding up future forest breeding programs with the aim of sustainable woody biomass production. For example, the use of genome-wide selection is an emerging approach that will revolutionize the applications of tree breeding. Phenotypic selection or marker-assisted breeding protocols can be replaced by selection, based on whole-genome predictions

in which phenotyping updates the model to build up the prediction accuracy. Ultimately, GS could substantially shorten generation time through rapid cycles of breeding, selection and propagation.

Second-generation biofuels produced from forest lignocellulosic biomass represent a renewable, more carbon-balanced alternative to both fossil fuels and corn-derived or sugarcane-derived biofuels. However, forest biomass recalcitrance to saccharification is one of the major impediments to high-yield and cost-effective production of biofuels and value-added bio-chemicals and bio-materials from lignocellulosic feedstocks. Due to the natural recalcitrance of lignocellulose, coupling forest and industrial biotechnology will further improve the conversion process from biomass to second-generation biofuels and bio-products (Fig. 2 and 3). Decreasing lignin content and/or modifying lignin monomer composition of forest biomass by genetic engineering is believed to mitigate biomass recalcitrance and improve conversion efficiency of tree biomass. Likewise, industrial biotechnology involving sequencing the genomes of natural microbes will lead to important insights relevant to biofuels production. Lignin degradation in nature may provide novel resources for the delignification of forest lignocellulosic biomass feedstocks. It is strongly believed that the genome of these microorganisms encode hundreds of enzymes potentially dedicated to lignin degradation. Finally, a better biosafety regulation over the momentous tree genetic engineering and novel breeding technologies and their long-term economic impact would bring valuable contributions towards developing an economically sustainable biofuels and biomaterials markets worldwide.

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