Allo- and Xenotransplantation without Immunosuppression: Lessons from Horticulture in Comparative Biology

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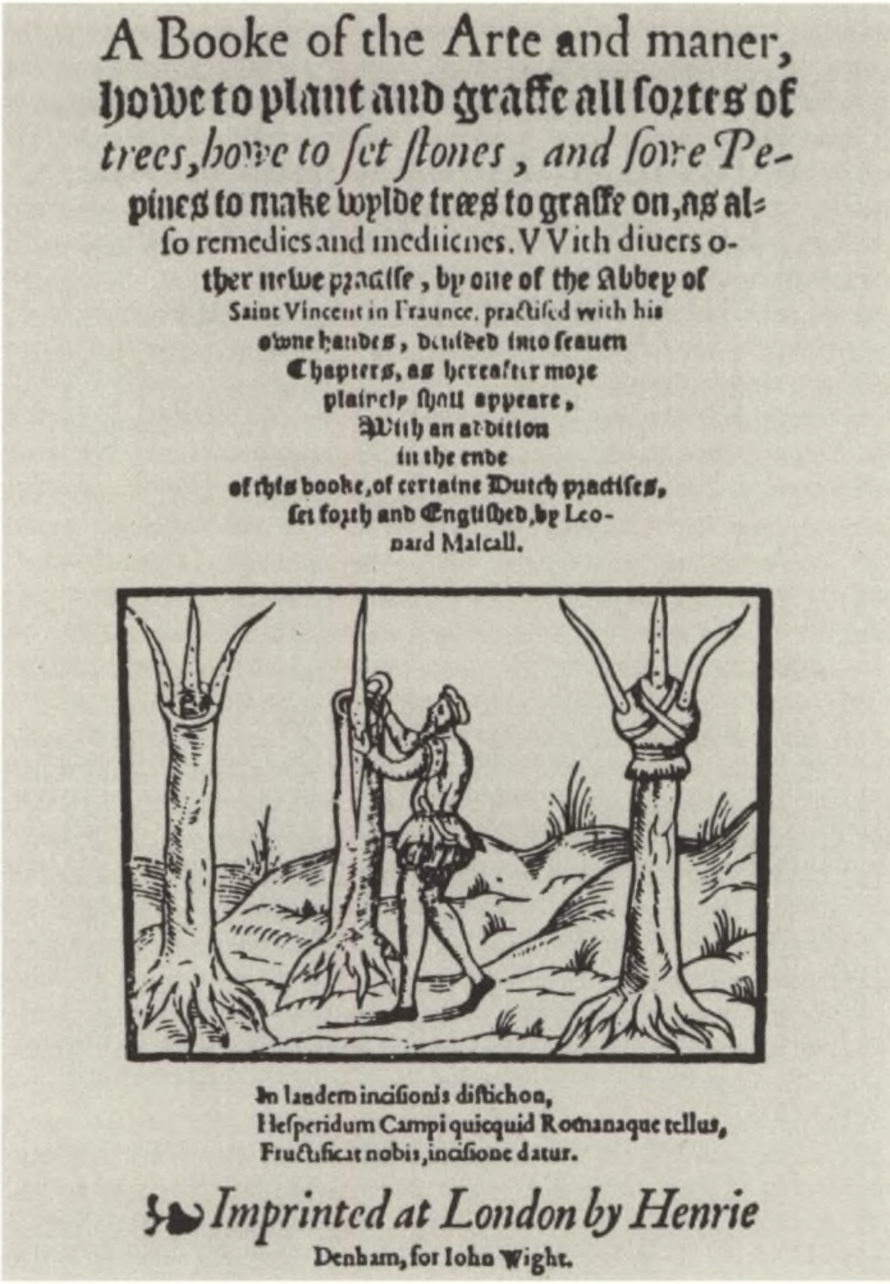
I chose the topic of transplantation in the Vegetable Kingdom for three reasons: 1) It successfully preceded transplantation in the Animal Kingdom by several centuries; 2) One of my childhood heroes was Luther Burbank, who became a household name as a plant transplant surgeon at the turn of the century; and 3) I thought it would be fun. I did not know much about plant grafting, but I always had a green thumb. Therefore, I took a course in the College of Agriculture at the University of Minnesota (Horticulture 101: Plant Propagation) to prepare for my address. One of my medical student advisees, Clayton Chau, helped me with the laboratory exercises and the homework, and Professor Peter Ascher (my instructor for the course) was most generous, engaging in discussion comparing transplants in his world (vegetable) and mine(animal).

I also had extensive discussions on comparative biology with my colleague Jeffrey Platt, whose main interest is xenotransplantation. He accompanied me on a trip to the University of Minnesota landscape arboretum, where I photographed several examples of tree grafts for my talk. Some were xenografts (even highly discordant ones can sometimes succeed in the plant world).

I spent several hours in the arboretum library, not only browsing but also running with my findings to horticulture professor and curator Michael Zins for more discussion on comparative transplant biology. Numerous horticulture publications on plant grafting have appeared since the invention of the printing press, and I used examples from many in my lecture (Figure 1). The members of the ASTS should also be grateful to the science of plant propagation, since without it we would not be able to enjoy the French wines we do today. *Phylloxera vastatrix* (a root louse) destroyed most of the


A Booke of the Arte and maner,
howe to plant and graffe all ſortes of
trees, howe to ſet ſtones, and ſowe Pe-
pines to make wylde trees to graffe on, as al-
ſo remedies and mediicnes. VVith diuers o-
ther newe practiſe, by one of the Abbey of
Saint Vincent in Fraunce, practiſed with his
owne handes, deuided into ſeauen
Chapters, as hereafter more
plainely ſhall appeare,
With an addition
in the ende
of this booke, of certaine Dutch practiſes,
ſet forth and Engliſhed, by Leo-
nard Maſcall.

In laudem inciſionis diſtichon,
Heſperidum Campi quicquid Romanaque tellus,
Fructificat nobis, inciſione datur.

Imprinted at London by Henrie
Denham, for Iohn Wight.

Figure 1. Suggested Reading

French vineyards in the 19th century. The vineyards were rescued by grafting French vines onto California grape roots that were resistant to this louse.

In my address I went into the science of plant propagation, with emphasis on inter- and intraspecies grafting. Without the techniques developed several centuries ago, we would not have a uniform supply of apples, oranges, plums, and other fruits we so much enjoy. Most seedlings give scrub fruit. Useful varieties must be propagated by grafting. The science of plant propagation is as useful—if not as complex as—the science of immunology, but it is too much to reiterate here.

Grafting is used for plant propagation to perpetuate a true variety whenever this cannot be accomplished by seed propagation or rootings of cuttings. A variety of surgical techniques are available. Today, propagation can be accomplished by cellular engineering as well. Although all grafted plants are chimeric in the Greek mythology sense, in horticulture the term is usually reserved for plants whose tissue consists of intermingled cells of more than one genotype.

Much of the terminology in plant propagation is similar to that in transplant immunology. For example, there are clones, and a clone can evolve within a variety that has been cultivated vegetatively for a long time. Members of a vegetative clone have the same genotype until spontaneous mutations occur, as is the case in the animal world. Selection is the most effective process by which plant breeders (propagators, grafters) alter the traits of cultivated (cloned) plants, in conformity with human desires.

Clonal selection is based on the recognition and the isolation and evaluation of biotypes of a polyclonal variety. The methods are similar to those we use, with in vitro experiments leading to in vivo application.

The terms encountered in textbooks of plant propagation are familiar. Compatibility and incompatibility are well described. Are graft compatibilities and incompatibilities exhibited in the vegetable world (allo- and xeno-) relevant to those in the animal world? Intraspecies grafts take easier than interspecies grafts, but there are examples of the latter in which a take is a regular occurrence. Tendency toward this occurrence is termed affinity (the behavior of the scion toward the root stalk in the grafted stage). Some grafts will survive for years, and then wither. Is delayed incompatibility of plant grafts akin to chronic rejection of animal grafts?

Plant grafts are free grafts, but become neovascularized (yes, plants do have vascular systems). Do plants have an immune system? Yes, at least a primitive one. There is a cellular response to injury with proliferation, walling off, and healing.

Just as in our world of transplantation, horticulture is filled with personalities and characters. Luther Burbank is only one example. He was born in 1849 and died in 1926. He exhibited several traits in common with our members: passion and ego. He once said, "See, I am about the same height as Napoleon and my hat is about the same size as his, although my head is growing and increasing in size all the time." Burbank was the epitome of a scientist who followed Pasteur's dictum: Chance favors the prepared mind.

Burbank immigrated from Massachusetts to Santa Rosa in Sonoma County, California, in 1875 to become nurseryman extraordinaire. (I am indebted to John Rabkin for making a trip to Santa Rosa to collect memorabilia for my talk.) Before leaving Massachusetts, he had developed the Burbank potato by sheer luck from a rare seed ball, whose descendants included both the Idaho and the Main. In 1881, Burbank produced 20,000 prune trees for setting out in one season by grafting onto growing Almond stock. His first commercial success gave him capital for continuous experimentation. He tried and succeeded with extremely discordant grafts that others had assumed would not work. He dismissed critics with words such as, "Orthodoxy is ankylosis, no one at home; ring up the undertaker for further information."

The Idaho potato has been with us now for more than a century. Even older chance occurrences are easily identified. We all love the Bizzaria orange, half-orange, and half-citron. This originated from an adventitious bud from the callus of a sour orange graft on a citron in Florence, Italy, in 1644, and has been perpetuated vegetatively to the present. We owe it to an observant Medici.

Well, what about the science? What determines plant grafts' compatibility and incompatibility? When opposing cells touch, their walls dissolve and holes appear. The plasmalemma contact each other and release protein molecules that form catalytic complexes. These complexes determine graft compatibility. An example of an incompatible situation is between the pear and the quince. β-glycosidases from pear hydrosylases liberate cyanide from quince prunasin, causing developmental abnormalities at the graft interface and inhibiting union. I would rather deal with T cells than cyanide. Symbiotic relationships between viruses in certain plants can also lead to incompatibilities. Some viruses have a symbiotic relationship in the root stock, but when transferred to a scion have a pathological effect on the graft.

Nonimmune incompatibilities predominate in the world of vegetable grafts. Analogies to animal grafts can be made (nutritional, enzymatic, physical). In the Vegetable Kingdom, a fundamental biological incompatibility that would not support xenotransplantation, even when the immunological problems are solved.

On the other hand, graft-host affinities are common in the vegetable world. The probability of affinity is higher between closely related species (concordant). In what would otherwise be predicted to be discordant combinations, useful exceptions occur.

Is there a lesson in the extremely discordant successful grafts? The most extreme, of course, would be grafting from a vegetable to an animal or an animal to a vegetable. Could a tree stump survive by nutrient diffusion and continuously grow to replace the end chafed by a Captain Ahab stomping on the deck of his ship? Well, I will leave that puzzle to the ASTS members now leading us into the brave new world of xenotransplantation.