conducted 1 year later and consisted of a behavioral assessment (determining episodes of unprotected intercourse and consistency of condom use) as well as health outcomes, defined by reported and recorded rates of sexually transmitted disease (STD) symptoms and diagnosis of new and repeated infection with chlamydia and gonorrhea. The study design ensured consistency across settings for evaluation and outcome criteria. This study is a good example of a large, well-designed intervention study with an adequate period of follow-up and relevant outcome criteria, including both behavioral and STD end points. This type of intervention, namely small group meetings as a means to alter individual behavior, is one that could be instituted in many health-care settings, including managed care, public programs, and school or community-based settings.

The approach used in Thailand takes this intervention strategy to the next level (*3*). The premise of this HIV prevention process is that changing individual behavior is necessary, but not sufficient, for decreasing the risk of HIV infection. Instead, the focus of the intervention was widened to include the cultural context in which individuals are living. The intervention thus included a strategy to saturate the public with information about the safety and efficacy of condom use, and to use government funding to make 60 million condoms available to the population. The implementation required not only cooperation from the public health sector, but contributions from the social and economic sectors as well. The government invested 2 billion baht in the program in 1997. The rates of HIV infection in two groups were documented before, during, and after the campaign. Rates of infection were rising rapidly before the intervention, fell considerably during the time of the campaign, and are now beginning to rise once again, in part because of the financial crisis in Thailand (and in Asia generally), which has severely curtailed the availability of funds for the continuation of the prevention efforts. So, "Does HIV prevention work?" The answer is, "yes—but one always needs to be able to actually implement the intervention." This requires access to services for evaluation and treatment, a supportive community or environment to enable individuals to actually carry out the healthful behaviors, and the ability to acquire the information, skills, and services to reduce risk.

So why don't we benefit from what we know works? In the United States, politics interfere with science-based policy. The administration recently acknowledged the scientific basis for recommending needle exchange programs as a useful way to reduce HIV transmission by intravenous drug users and their partners, but its withholding of federal funding for these efforts shows the effect of politics. Similarly, Congress assigned $50 million in 1997 for abstinence-only education, at a time when a fuller, more balanced approach was shown to be more effective. Comprehensive family life and sex education with age-appropriate access to condoms is a far better approach to reduce risk-related behaviors in students. In addition, the major television networks continue to ban condom advertisements, despite the recent Kaiser Family Foundation survey showing that 72% of adults support condom commercials on network TV. So a major obstacle to effective HIV prevention is not a dearth of good ideas or scientifically based interventions, but rather political restraints, even where adequate science exists as a basis for policy recommendations.

The answer to the third question is therefore "AIDS prevention efforts in the United States compare poorly to those of other nations." Clearly, the United States has the resources to provide necessary interventions and services suggested by the scientific studies of HIV prevention. Now is an appropriate time to question both the cost and quality of HIV prevention efforts, but there is little evidence that the United States is doing so (*4*). Other countries, such as Switzerland, Australia, and most Western industrialized nations, have far lower HIV rates and unintended pregnancy and STD rates than those reported in the United States. One study of the cost-effectiveness of HIV preventive efforts compared three interventions (*5*). The study examined the estimated cost per HIV infection averted. Variables included the number of uninfected individuals, the incidence of HIV, the effectiveness in reductions in risk behaviors, and the estimated number of HIV infections averted. The results pointed to clear differences in cost-effectiveness: $2,667 for needle exchange for injection-drug users (in New York City); $12,000 to train community leaders (in Biloxi, Mississippi); and $194,186 for HIV testing of surgeons. The United States has the money but does not invest it wisely, according to this analysis. Scientifically based prevention strategies exist, they work, and they are available to scale up to larger populations—but only if we can align policy and politics with the current science of HIV prevention.

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PLANT BIOLOGY

How Calcium Enhances Plant Salt Tolerance

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Like cells in general, most plant cells accumulate the ion potassium and exclude sodium. The resulting high potassium/sodium ratios in the cells enable potassium to perform essential functions that sodium cannot fulfill. This selectivity in favor of potassium is especially important in the arid and semi-arid regions of the world, where excess sodium salts in the soil cause widespread and often severe problems for crop production. The sodium may compete with potassium in membrane transport and in functions such as enzyme activation, impairing the ability of the plant to grow. For decades, it has been known that another ion, calcium, is required to maintain or enhance the selective absorption of potassium by plants at high concentrations of sodium (*1*). The mechanisms underlying this crucial action of calcium in protecting plants against the disruptive effects of high sodium concentration have so far eluded us. Now on page 1943 of this issue, a significant advance in our understanding has been made by Liu and colleagues (*2*), who have identified the molecule that likely mediates this calcium protection.

During membrane transport of ions in any plant exposed to saline conditions, potassium/sodium discrimination is critical at several steps (see the figure). Absorption of potassium initially occurs by an epidermal or cortical cell of the root as it is transported across the outer cell membrane or plasmalemma. After this radial transport across the root, the ion is then delivered into the conducting system of the xylem, in

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which the element is moved toward and into the shoot. The xylem vessels are apoplastic [that is, composed of extracellular (cell wall) matrix and space], so delivery into this system requires an efflux step, from root cell cytoplasm or "symplast" into the vessels. Movement of potassium and other nutrients takes place in the "transpiration stream," the movement of water that is ultimately driven by the evaporation or "transpiration" of water, mainly from leaves. Upon arrival in the apoplastic space of the leaf, if it is to function in cellular metabolism, potassium must once again be transported, this time across the plasmalemma of a leaf cell into its cytoplasm. At this point there may be, in addition, redistribution of potassium, most commonly from older to younger, actively growing leaves. This redistribution takes place via the phloem, a cytoplasmic pathway.

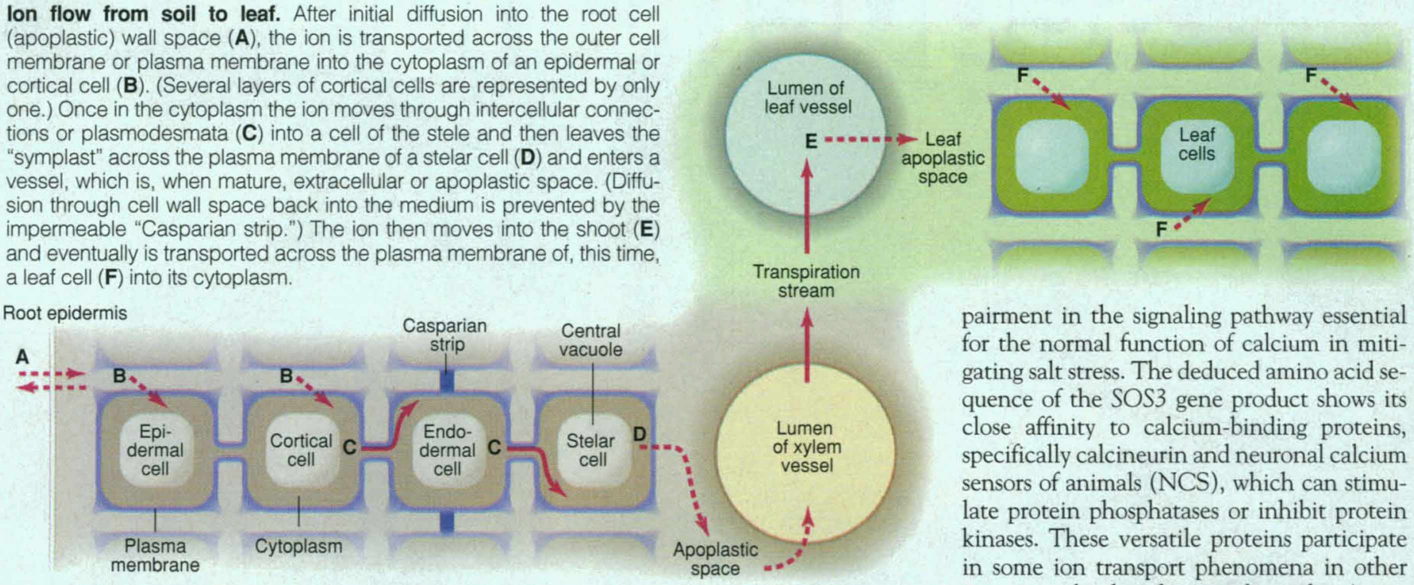
Nor is that all. At three other potassium transport steps, the plant must differentiate between sodium and potassium. First, inside the cell, potassium is partitioned between the cytoplasm and the vacuole, across the intervening membrane, the tonoplast. While the cytoplasmic potassium concentration is under rather tight homeostatic control, that of the vacuole is more variable. Second, potassium is a major osmoticum of plant cells, an especially crucial feature for plants under high-salt conditions, and one requiring controlled partitioning of the element among organs, tissues, and cell compartments. And third, potassium plays a central role in the opening and closing of stomata, the pores that regulate gas exchange between leaves and the atmosphere. The ion is shuttled into and out of the guard cells, thereby controlling the osmotic movement of water into and out of these cells and, hence, the size of the stomatal aperture and the transpiration rate.

These potassium transport steps are multifarious and complex, and it is likely that all are sensitive to calcium concentrations in the cell. However, because the internal calcium status cannot be manipulated and monitored, most experiments investigating the role of calcium in potassium/sodium transport have had to test the absorption of potassium at various concentrations of potassium, sodium, and calcium in the medium in which the plant roots are bathed. Transport of the ions to the shoot, most often the extent of sodium exclusion from it, is often included.

Experimentation with these methods had reached, or at least approached, a point of diminishing returns in unraveling potassium/sodium transport and salt toleration (and eventually improving plant salt tolerance). Enter the techniques of molecular biology. As a result of the application of molecular biology to this field, several genes and gene products for potassium transport have now been identified and characterized (3). Some operate as high-affinity (mechanism 1) transporters or carriers, whereas others function as low-affinity (mechanism 2) channels (4). How are these regulated by calcium? It is unlikely, given the multiplicity of the sites of potassium/sodium discrimination mentioned earlier, that calcium plays only one role in potassium transport and potassium/sodium selectivity. Rather, responses to salt stress are mediated by signaling pathways in which calcium acts as a second messenger. It is here that the new work contributes.

Now, Liu *et al.* provide a molecular basis for the calcium sensitivity of potassium/sodium discrimination. In *Arabidopsis* plants carrying a mutation in the *SOS3* gene, the ratio at which potassium and sodium are accumulated is changed to lower potassium/sodium values than in wild-type plants, and the operation of the high-affinity potassium transporter is suppressed. Both abnormal functions are mitigated or abolished by high external calcium concentrations, suggesting that in the mutants there is an impairment in the signaling pathway essential for the normal function of calcium in mitigating salt stress. The deduced amino acid sequence of the *SOS3* gene product shows its close affinity to calcium-binding proteins, specifically calcineurin and neuronal calcium sensors of animals (NCS), which can stimulate protein phosphatases or inhibit protein kinases. These versatile proteins participate in some ion transport phenomena in other organisms, lending force to the authors' conclusion that the gene *SOS3* mediates the interaction of potassium, sodium, and calcium.

The authors have provided a molecular view of the earlier physiological findings that pinpointed the essential part that calcium plays in potassium/sodium discrimination in plants. The potential of this discovery to advance the pressingly important enterprise of developing salt-tolerant crops is considerable, notwithstanding the fact that *Arabidopsis* is not itself a salt-tolerant plant. Next, we will need to address the problem of which sites, among the many where potassium/sodium selectivity comes into play, are affected by this gene.



Ion flow from soil to leaf. After initial diffusion into the root cell (apoplastic) wall space (**A**), the ion is transported across the outer cell membrane or plasma membrane into the cytoplasm of an epidermal or cortical cell (**B**). (Several layers of cortical cells are represented by only one.) Once in the cytoplasm the ion moves through intercellular connections or plasmodesmata (**C**) into a cell of the stele and then leaves the "symplast" across the plasma membrane of a stelar cell (**D**) and enters a vessel, which is, when mature, extracellular or apoplastic space. (Diffusion through cell wall space back into the medium is prevented by the impermeable "Casparian strip.") The ion then moves into the shoot (**E**) and eventually is transported across the plasma membrane of, this time, a leaf cell (**F**) into its cytoplasm.

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