Angiostatin's Partners

The degree of change in the grizzly bear population in Yellowstone National Park is said to be in dispute. An adviser to the Chief U.S. Forester points out that "[p]eople [in the United States] no longer view national forests solely as a warehouse of commodities to be brought to market." The implications of angiostatin's binding of ATP synthase on the surface of human endothelial cells are discussed. The climber's view of conserving cliff ecology is presented. And how 7-month-old infants learn the rules of language is debated.

Yellowstone Grizzly Population

The News Focus article "A species' fate, by the numbers" by Charles C. Mann and Mark L. Plummer (2 Apr., p. 36) is generally a good synopsis of the recent population viability (PVA) workshop in San Diego. They state, however, that the Yellowstone grizzly bear population has been increasing by 5% per year and that some experts say the bear could be removed from the endangered list. If only it were so. Unfortunately, both the numbers of bears and the rate of change in those numbers in the Yellowstone ecosystem are in dispute. Like Mark Twain's death, the "rumors of recovery" for the Yellowstone grizzlies may be highly exaggerated. Interested readers should look for an al-



The grizzly population at Yellowstone National Park may not be increasing.

ternative analysis in a forthcoming article by Craig Pease and David Mattson in an upcoming issue of the journal *Ecology*. Most of the apparent increase has occurred since the fires of 1988 burned a good portion of the ecosystem. Bears may simply be more visible, or may be in new territory because their old feeding grounds are in the process of growing back after the fires. While I would like to think that PVA has made a

tangible contribution to conservation efforts, I fear that the jury is still out on the real status of the first population to which these concepts were applied.

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Managing the National Forests

In an otherwise informative article by Charles C. Mann and Mark L. Plummer about the report of the Committee of Scientists relative to management of the U.S. National Forest System ("Call for 'sustainability' in forests sparks a fire," News Focus, 26 Mar., p. 1996), I am quoted as saying that "most folks have so much disposable income that they are looking at forests in terms of the positive outcomes of good stewardship like biodiversity, like tourism, like existence values...." While this may have been the most provocative and pithy part of my interview, the context is, unfortunately, lost.

Developing countries exploit their natural resource base, often in an unsustainable manner, in order to improve their standard of living. It is a strategy that rarely works. We in this nation have the highest standard of living the world has ever known, with so much disposable income available that we can afford to make investments in conservation. People no longer view national forests solely as a warehouse of commodities to be brought to market. Greater value is assigned to the positive outcomes of good stewardship like biodiversity, tourism, clean water, existence values, and an ecologically sustainable flow of goods and services.

To a certain extent, the whole debate over sustainability is academic. The U.S. Forest Service's commitment to sustainability is well established in tradition and law. Ecological sustainability frames the decision space from which we make economic and social choices. This is also a matter of common sense, as we simply cannot meet the needs of people without first securing the health of the land.

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I am writing to comment on Marcia Barinaga's article "A surprising partner for angiostatin" (News of the Week, 19 Mar., p. 1831). She describes a paper by Tammy Moser and her collaborators ("Angiostatin binds ATP synthase on the surface of human endothelial cells") (1) that indicates that angiostatin binds to the alpha and beta subunits of the mitochondrial adenosine triphosphate (ATP) synthase, presumably at the surface of endothelial cells. The authors further suggest that binding of angiostatin to the alpha and beta subunits of the ATP synthase may mediate its anti-angiogenic effects. This is indeed a remarkable finding because up until now we have believed that the usual place for F₀/F₁ ATP synthase is in the mitochondria, not in the plasma membrane of normal cells. Indeed, endothelial cells can grow in low-oxygen environments, such as tumors. It is well known that the extracellular pH of tumors is very acidic. Acidic extracellular pH is under most circumstances unfavorable for



Fluorescently labeled antibodies (red) show ATP synthase on human endothelial cells.

growth. Under these conditions, one would expect that tumors and endothelial cells might exhibit alternative pH regulatory mechanisms to allow proper cell survival and avoid intracellular acidosis. We have suggested that tumor cells accomplish this by means of plasmalemmal vacuolar-type proton adenosine triphosphatase (V-H⁺-ATPase) (2). This enzyme normally resides in acidic organelles and works to maintain an acidic environment in endosomes and lysosomes. When located at the plasma membrane, this pump works to extrude acid. In highly invasive and metastatic tumor cells, this proton pumping activity is exacerbated (3). We have preliminary evidence that microvascular endothelial cells involved in angiogenesis also exhibit plasmalemmal V-H⁺ATPase at the leading edge (4). Because of the remarkable similarities in structure and subunit composition between V-H $^+$ -ATPase and the F_0/F_1 ATP synthase, it is interesting that proton pumps usually believed to be located in intracellular organelles (V-H+-ATPase in endosomes and

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