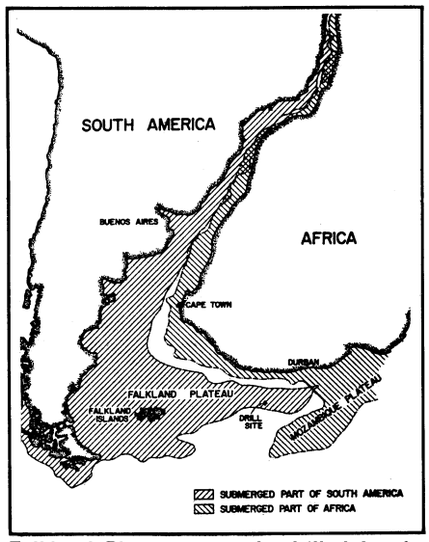
Challenger rounds the Horn

Buffeted by giant swells and imperiled by icebergs, the deep sea drilling ship *Glomar Challenger* rounded Cape Horn in January to seek the nature of the Falkland Plateau, a submerged ridge that lies like the remnants of an ancient umbilical cord between South America and Africa.

The Falkland Plateau extends 1,000 miles eastward from the coast of Argentina. The Falkland Islands, 500 miles from the Argentine coast, mark the western extreme of the plateau; on the eastern cusp lies a submerged rise known as the Ewing Bank. Core samples from Leg 36 of the Deep Sea Drilling Project confirmed in 1974 that the plateau was once attached to the Agulhas Bank of Africa and that it foundered when South America and Africa split (SN: 7/27/74, p. 54). The recent voyage to the plateau, Leg 71, planned to flesh out the picture of the plateau's structure and its role as a barrier to water flow into the early South Atlantic.

According to co-chief scientist William J. Ludwig of Lamont Doherty Geological Observatory, the coring was abbreviated by the weather, but the journey still provided the necessary "ground truthing" for earlier seismic exploration of the area. For example, seismic profiles — obtained by bouncing sound waves off the sea floor — showed that the basin between the islands and the Ewing Bank is probably not made of continental crust. One of the two deep cores taken by Leg 71 confirmed that the basin rock is oceanic in origin. This indicates, Ludwig explained, that the continental connection between the islands and the bank may lie along the escarpment between them.

The core samples also provide pictures of the early southern Atlantic Ocean and of climate changes in the region as the two continents slowly rumbled on their opposite paths. Organic-rich black shales, dating about 180 million years old, indicate a shallow-water, restricted environment — meaning that the south Atlantic was a stagnant pond when the continents began to separate. The disappearance of the black shales and the presence in the core samples of fossils typical of oxygen-rich water indicate increased circulation of water about 135 million years ago. More sediments accumulated as the plateau sank deeper about 80 million years ago. At the point in the core samples corresponding to 65 million years ago, Ludwig and co-workers found a halt in the deposition of sediments and evidence of deep erosion across the plateau. This indicates, he says, that a sudden rush of bottom water flowed into the new sea from the south, possibly as a result of a break in Antarctica as it drifted away. The opening 45 million years ago of the Drake Passage between South America and Antarctica is similarly marked in the cores, Ludwig says. To complement work in the southwest Pacific, Leg 71 also recovered a record of the fluctuations in water temperature around Antarctica. Such information, says Ludwig, may aid climatologists in understanding why the region, once as balmy as the Mediterranean, became glaciated. □



Columbia Univ.

Falkland Plateau, recently drilled by the Challenger, *is a continental remnant that sank as South America and Africa drifted apart approximately 135 million years ago.*

How sweet it is: Saccharin update

Although the artificial sweetener saccharin has not reached the end of the risk-assessment obstacle course that continues to frustrate scientists, legislators and the public, it recently cleared several evaluative hurdles — human case-control studies. In fact, the results of these case studies support an earlier finding (SN: 1/5/80, p. 6) that saccharin may not be the potent initiator of bladder cancer it was once thought to be (SN: 3/3/73, p. 133).

One study, conducted by Ernest L.Wynder and colleague of the American Health Foundation, involved 302 male and 65 female bladder cancer patients in New York hospitals and 367 controls matched to them in age, sex, hospital and hospital-room status. Wynder and co-worker classified artificial sweetener users on the basis of whether they had consumed at least 40 to 80 milligrams of saccharin (canned diet beverages contain about 8 to 11 mg per ounce) for at least 10 years. The results, reported in the March 14 SCIENCE, indicate no statistically significant difference between case and control groups classified in this manner. Furthermore, the researchers found no evidence of saccharin as a promoter of tobacco-smoking-related cancer.

In another study, reported in the March 6 NEW ENGLAND JOURNAL OF MEDICINE, Alan S. Morrison and colleague of the Harvard School of Public Health gathered the history of artificial sweetener use from 592 patients with lower urinary tract cancer and from 536 controls in the Boston area. While the researchers found that men who consume more than three artificially sweetened drinks per day have a greater risk of developing urinary tract cancer than do men who consume less, the reverse was found in women. "The results of this study," the researchers report, "suggest that, as a group, users of artificial sweeteners have little or no excess risk of cancer of the lower urinary tract."

Morrison and colleague say their results can be interpreted in several ways. "One is that the exposures that have been sustained to artificial sweeteners are not carcinogenic for the human bladder." A second interpretation is that the carcinogenicity of the sweeteners is too weak for its effects to be perceived. Finally, the researchers say, "More time may be necessary for accumulation of carcinogenic level of exposure."

Meanwhile, writes Robert Hoover of the National Cancer Institute in a March 6 JAMA editorial, decisions regarding saccharin consumption must be made, even though the controversy is not resolved. "When all the evidence of toxicity is weighed against the lack of objective evidence of benefit," he says, "any use by nondiabetic children or pregnant women, heavy use by young women of childbearing age and excessive use by anyone are ill-advised and should be actively discouraged by the medical community." □

Scale up for new, old gene-splice products

Laboratory bacteria have now been engineered to produce two more materials that are naturally made only by human cells, and large-scale production of such substances appears imminent. At the meeting of the Recombinant DNA Advisory Committee at the National Institutes of Health on March 7, the South San Francisco research firm Genentech requested permission to scale up to 750 liters bacterial production of five human substances.

Two new achievements of the recombinant DNA technique were included in Genentech's request. One is bacterial production of thymosin alpha-1, a hormone that stimulates the human immune system and may help the body resist disease. Thymosin alpha-1 has shown promise in clinical trials for the treatment of brain and lung cancer, the Genentech scientists say, although only small amounts of the hormone, synthesized chemically, have been available. Genentech says the recombinant DNA method potentially could increase considerably availability of thymosin alpha-1 by the end of 1980.

Genentech's second announcement at

the meeting was bacterial production of human proinsulin. This natural precursor of insulin contains both chains of the amino acids that are joined to make the hormone. In previous work, Genentech-sponsored scientists had modified separate bacteria to make each chain (SN: 9/16/78, p. 195). Production of insulin from proinsulin is an alternative strategy that may be technically simpler than the combination of two separate chains and purification of the insulin product. The company also requested authorization to scale up new procedures for producing the two separate insulin chains and the human hormone somatostatin (SN: 11/12/77, p. 310). Genentech had been authorized previously for large-scale production of those three substances and also for human growth hormone.

At the closed session of the advisory committee meeting, the pharmaceutical company Eli Lilly also asked for further scale-up authorization for insulin. In addition, Schering-Plough pharmaceutical company requested authorization to scale up bacterial production — probably of interferon (SN: 1/26/80, p. 52).

In other action, the advisory committee decided that a set of safety guidelines written for large-scale recombinant DNA operations would be published in the FEDERAL REGISTER for public comment, and the members argued whether industrial authorizations should be handled through the Occupational Safety and Health Administration, instead of through the NIH committee. □

Interferon bandwagon

Although interferon is still too scarce and too expensive to be proved an effective drug, hints that the substance can fight both viral infections and cancer have led the drug industry to invest millions of dollars in pursuit. Among the latest announcements are those from Abbott Laboratories of Chicago and G.D. Searle and Co. of Skokie, Ill. Abbott says it will use a tissue culture technique developed for another drug to produce fibroblast-type interferon. Searle announced it also has new technology for growing fibroblast cells in tissue culture for interferon production. Searle says it plans to construct a $12 million pilot plant in England to make interferon and other biological therapeutics. This month Searle will begin supplying scientists at the University of Texas with interferon for the first large-scale (30-patient) evaluation of fibroblast interferon as cancer therapy. While stepping up their tissue culture methods, both Searle and Abbott claim to have the resources and expertise to convert, if it becomes expedient, to recombinant DNA techniques, which have already been demonstrated capable of making small amounts of another type — leukocyte — interferon (SN: 1/26/80, p. 52). □

Kinetics: Enter laser, spectrometer

Lasers have performed in a number of analytical duets over the years: They have teamed up with cloud (SN: 5/26/79, p. 343) and combustion (SN: 9/15/79, p. 188) chambers, for example, for the study of various chemical processes. Now, John T. Herron and colleagues of the National Bureau of Standards are experimenting with another useful partner for the laser — a mass spectrometer.

Herron and co-workers recently coupled an infrared-laser to a mass-spectrometer to study the kinetics — or rate — of complex chemical reactions in real time. "Most chemical processes of importance are controlled by kinetic factors [such as temperature or concentration of reactants]," explains Herron. Furthermore, these processes all involve intermediates: "You don't just go from A to C; you go from A to B to C, where B is the intermediate." The laser in Herron's system breaks the A molecules into the B's, or free-radical intermediates — molecules with an odd number of electrons in the outermost principal energy level.

But, says Herron, "You not only have to be able to make the free radicals using an infrared laser, you also have to have a way of following them in real time. In this case we are using a mass spectrometer."

Mass spectrometers, the "watchdogs" of chemical reactions, continually monitor which free radicals are formed and how fast they disappear. The instrument capitalizes on a molecule's unique mass to charge (m/e) ratio: The m/e signals received by the spectrometer from a particular reaction chamber identify the free radicals in that chamber and the intensity of the signals indicate the abundance of free radicals.

Coupled with a laser, the spectrometer becomes part of Herron's new chemical kinetics technique — infrared-laser photolysis/mass spectrometry — which he hopes to apply to the study of photochemical smog formation, chemical reactions of the stratosphere and combustion. "We're getting into an era of chemistry in which we have to understand biomass and coal processes, for example, and those are very complicated," Herron says. "That's the kind of chemistry we're interested in attacking." □

Disease carriers and lowered IQ

It's not surprising that victims of certain inherited metabolic diseases suffer brain damage as one of their symptoms. But what is surprising is the apparent finding that carriers of at least one of these disorders also suffer brain damage on occasion and, even more intriguing, that the damage the carriers incur sometimes consists of subtle drops in IQ. So report Mark L. Batshaw of Johns Hopkins Medical Institutions and his colleagues in the Feb. 28 NEW ENGLAND JOURNAL OF MEDICINE.

Males who inherit an X chromosome-linked deficiency in the enzyme ornithine transcarbamylase are unable to correctly metabolize protein and as a result suffer vomiting, coma and even death. Females who carry one gene for the enzyme deficiency and one normal gene, sometimes, but not always, show symptoms of the disease as well, notably mental retardation. Batshaw and his team have now tested the hypothesis that even largely asymptomatic carriers of this enzyme deficiency may suffer some subtle brain damage as a result of their carrier state.

The researchers zeroed in on four generations of a Mormon family in which 12 males had died of an ornithine transcarbamylase deficiency. They tested 18 females in the family to see whether they were carriers of the enzyme deficiency and found that seven were. Then they examined the seven women and six of their sisters neurologically and psychologically. Results were analyzed for evidence of cerebral dysfunction by four psychologists who were unaware of the purpose of the study and thought it was set up.

The psychologists found no significant differences between the carriers and their sisters on visual perception, memory and academic performance tests. In addition, the carriers' neurological exams were within normal limits. Their IQs, however, were an average of 5.6 points lower than those of their healthy siblings — a statistically significant difference. In fact, the carrier with the lowest IQ showed the most pronounced indication of enzyme deficiency (high levels of ammonia after eating protein), while the carrier with the IQ closest to those of the healthy subjects showed the least indication of enzyme deficiency. So it appears that carriers of ornithine transcarbamylase deficiency may suffer lower IQ because of excesses of ammonia in their bodies.

"This is particularly interesting," Steven Matthysse, a physician with McLean Hospital in Belmont, Mass., writes in an accompanying editorial, "because almost nothing is known about the role of metabolism in differences in IQ within the normal range of scores." It is possible, he says, that carriers of other metabolic disorders may also suffer cerebral dysfunction — say a drop in IQ or even psychosis. In 1966, in fact, a researcher reported a high frequency of psychotic disturbances in families that included some members afflicted with the inherited metabolic disease homocystinuria. That carriers of the inherited metabolic disorder phenylketonuria are at an increased risk of schizophrenia has also been proposed. □