

designer estrogens, O'Malley says.

"Different shapes [of the receptor-estrogen complex] attract different regulatory molecules" that themselves activate different genes, he says. "This may also help explain why the same hormone affects different people differently. People have slightly different proportions of coactivators and corepressors."

One question that has perplexed researchers is, Why are estrogen receptors so flexible about the compounds they bind? The observation that estrogen does not exist in just one natural form, but several, may provide an answer. Scientists have long known about the natural variants but believed that they all have the same effect. New research suggests that each of these naturally occurring estrogens has a subtly different effect.

In a study of 30 postmenopausal women, one natural variant of estrogen, called dehydroestrone sulfate, was effective in preventing hot flashes. It did not, however, seem to lower the amounts of fatty acids in the women's blood, suggesting that this estrogen doesn't benefit the heart.

These findings indicate that naturally occurring estrogens work selectively, says

Andrés Negro-Vilar of Ligand Pharmaceuticals in San Diego. He and his colleagues reported their results in the June *JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM*.

"These data suggest that there are naturally occurring estrogens which can act as bona fide SERMs," says McDonnell. However, it will take a great deal of research to tease out their different activities, he says.

The more that basic research illuminates the natural function of the estrogen receptor, the better insight drug developers will have for creating new designer estrogens, he says.

Despite the progress scientists have made in understanding actions of designer estrogens, their long-term use is fraught with complications. "We're very excited about the potential of SERMs, but there is still a lot of work to do, especially on the long-term safety," cautions Franks. "To give a drug to a basically healthy person with the intention of preventing disease, you need to be very sure the benefits outweigh the risks."

Even the well-accepted benefits can be hard to weigh precisely. Despite many reports that estrogen therapy reduces heart disease, a U.S. study of almost 3,000 postmenopausal women who had already

had a heart attack found that those given hormone-replacement therapy were just as likely to die of heart disease as were women given a placebo, Stephen B. Hulley of the University of California, San Francisco and his colleagues reported in 1998.

"Overall, we don't know for sure whether raloxifene—or even estrogen—reduces heart disease," says Manson, although she suspects that both do. "It's going to be decades until we have a clear picture of all the benefits and risks of different SERMs."

One could make the case that until long-term trials are completed, physicians shouldn't prescribe any designer estrogen for extended use, she says. However, Manson also points out that few of the current drugs for preventing heart disease and osteoporosis have undergone long-term trials.

As the baby boomers reach retirement age, the need to judge the costs and benefits of hormone-replacement therapy presses on more women than ever before. If the promise of designer estrogens comes true, a woman's decision about whether to take a drug to combat postmenopausal health problems could become much simpler. Researchers agree, however, that there is no perfect designer estrogen—yet. □

Archaeology

Tool time in the Stone Age

Neandertals pursued a variety of toolmaking strategies in their settlements, showing an aptitude often attributed only to modern humans, according to an investigation of Stone Age artifacts in a Spanish rock shelter.

This finding adds to evidence that behaviors long assumed to have originated among modern humans beginning around 40,000 years ago actually appeared much earlier among other *Homo* species, including Neandertals (SN: 7/3/99, p. 4).

Manuel Vaquero of Universitat Rovira i Virgili in Tarragona, Spain, analyzed the spatial distribution of numerous stone implements from two sediment layers in northeastern Spain's Abric Romaní rock shelter. All the tools display a manufacturing style previously linked to Neandertals.

The upper soil layer, already dated at around 45,000 years old, shows signs of brief occupations by small groups, Vaquero contends. Stone tools and debris from toolmaking form three small clusters. Artifacts consist of relatively small, easily fashioned cutting instruments, each of which was prepared from start to finish at workstations set apart from other activities.

The lower layer, dated at about 50,000 years old, presents a contrasting picture of extended occupations by large groups, Vaquero reports in the September *ANTIQUITY*. Many stone-tool clusters surround a central accumulation, arranged so that large, sharpened flakes could be fashioned in stages at a succession of workstations. Toolmaking proceeded in areas also used for cooking and other domestic chores, another sign of long-term residence, Vaquero says.

In a related analysis of Stone Age tool traditions, Ofer Bar-Yosef of Harvard University and Steven L. Kuhn of the University of Arizona in Tucson conclude that elongated stone blades with sharpened points, often treated as an invention of modern humans around 40,000 years ago, appeared as early as 300,000 years ago among various members of the *Homo* lineage (SN: 4/11/98, p. 238).

Blades only came to dominate the archaeological record of western Europe and Asia, as well as parts of Africa, after 40,000 years ago, the researchers note. This may reflect manufacture of increased numbers of replaceable blades for tools with handles, Bar-Yosef and Kuhn proposed in the June *AMERICAN ANTHROPOLOGIST*. —B.B.

Well-aged slabs of art

Radiocarbon analysis of minute pigment samples taken from two painted rock slabs places their age at a minimum of 3,600 years, providing the oldest direct evidence for cave or rock art in southern Africa. European cave art dates back 30,000 years.

Scientists have surmised, based on the ages of associated finds, that people painted the walls of caves and rock shelters in this region as long as 27,000 years ago (SN: 10/5/96, p. 216). Until now, however, radiocarbon dates for rock-art pigments in southern Africa extended back 500 years at most.

Ongoing radiocarbon studies should continue to push back confirmed dates for southern African rock-art, say Antonieta Jerardino of the University of Cape Town, South Africa, and Natalie Swanepoel of Syracuse (N.Y.) University.

The scientists studied painted slabs unearthed in a burned deposit at Steenbokfontein Cave, located near South Africa's west coast. What remains of one scene shows three pairs of human legs and hips painted in red, with a white robe on one figure. The other depicts four red pairs of human legs and hips, with rows of white lines and dots on one set of knees and ankles.

A fire in the cave caused its walls to crack and dislodged the slabs, resulting in their burial, say Jerardino and Swanepoel in the August–October *CURRENT ANTHROPOLOGY*. The fire destroyed parts of the painted slabs and obliterated any images that had been painted on eight other slabs in the same deposit. —B.B.