sidestep that risk entirely by obtaining fetal cells from the mother's blood.

The first step was to confirm that fetal cells are actually present in the mother's blood—though in exceedingly low amounts—as several groups had suggested. The researchers did that by using polymerase chain reaction (PCR) techniques to detect and amplify a specific sequence of DNA from the Y chromosome, which presumably would come only from a male fetus. They were able to predict the sex of the child with 65% accuracy—"not an exciting number," as Wachtel concedes, but enough to convince them that fetal cells were indeed there.

Their goal was to find a way to enrich the concentration of those cells to get enough for prenatal diagnosis. For that the two groups used a flow cytometer, an instrument that uses laser light to separate cells according to different characteristics—in this case, on the basis of cell size, granularity, and the presence of two cell surface markers characteristic of fetal cells. The researchers then performed the same PCR analysis to see how well the enrichment worked: This time they were able to predict sex with 94% accuracy. Flow cytometry clearly works, says Wachtel, enriching the concentration of fetal cells from an estimated 1 in 20 million maternal cells to about 1 in 100.

Both groups then sent off their sorted fetal cells, fixed on glass slides, to Klinger to see whether they could actually be used for prenatal diagnosis with the new FISH technique. One slide from Wachtel and Elias' group contained cells from a woman who they knew, from CVS, was carrying a fetus with Klinefelter syndrome, a rare disorder in which males have two copies of the X chromosome. "When Kathy called and said we see an XXY male, we started to get excited," Wachtel recalls. Integrated Genetics also accurately detected a fetus with Down's syndrome from both groups.

But the "big splash," as Wachtel calls it, came when Wachtel's group sent a sorted sample from a 42-year-old woman who had not had CVS or amniocentesis. Integrated Genetics found the fetus carried three copies of chromosome 18, a syndrome that leads to severe mental retardation. That was the first time a prenatal disorder was actually diagnosed, rather than just confirmed, through this new approach, Wachtel says. He cautions, however, that "this is the first shot. It is certainly not ready for routine use yet." Indeed, his group has analyzed samples from just 41 women—far too few to determine either the specificity or sensitivity of the procedure. Klinger expects clinical trials to be under way within 2 years. "That is clearly where all of us would like prenatal diagnosis to go." ■ LESLIE ROBERTS

Brave New (RNA) World

Cambridge—The earliest days of life, many researchers now say, may have been played out in an "RNA world," in which one large molecule, RNA, carried out all the processes of life. But as acceptance of that idea spreads, its proponents are facing a new problem: How did the RNA world give way to the more complex biochemistry of life as we know it? That conundrum emerged as a key theme of Biological Functions of RNA, a symposium sponsored last week by the Whitehead Institute for Biomedical Research that was chock full of provocative notions.

The starting point for these notions—the theory of an RNA world—grew out of researchers' frustration at the seemingly neat division of labor in the realm of biomolecules. Protein enzymes do the heavy lifting, catalyzing the chemical reactions needed to sustain and reproduce life. DNA and RNA have it easier, serving mainly as a medium for the genetic information that guides all that heavy lifting. Life requires both functions, which seemed to imply that molecules filling both roles must somehow—defying all probability—have appeared at the same time in early evolution. But how?

That puzzle seemed on the way to being solved several years ago, when researchers found that RNA can play both roles: Besides storing genetic information, it can act as an enzyme. With that discovery, RNA began looking like a good candidate for being the primordial living molecule. But how would a swarm of specialized RNA enzymes have given way to a breed of proteins subsuming RNA's biochemical functions? At the Whitehead symposium, researchers presented startling evidence that RNA enzymes might well have fostered the transition by filling key niches in the world of proteins.

Molecular geneticist Alan Lambowitz of Ohio State University argued, for example, that one particular molecule that is a linchpin in the process of making new proteins may have evolved from an RNA enzyme. The evidence comes from a comparison between a present-day RNA enzyme found in the yeast *Neurospora crassa* and transfer RNA (tRNA), the linchpin molecule in question. tRNA is a shuttle that carries amino acids—the building blocks of proteins—to protein factories called ribosomes. By chance, Lambowitz and his colleagues found that a protein that binds to present-day tRNA molecules and attaches amino acids to them can also bind to part of the *Neurospora* RNA.

Lambowitz' interpretation of the result: Both RNA molecules must have the same three-dimensional shape, even though their sequences are very different. And that suggests to Lambowitz that some precursor of the RNA enzyme evolved into tRNA, and was thus recruited for protein synthesis.

Thomas Cech of the University of Colorado, a codiscoverer of catalytic RNA, raised the possibility of an even more active role for RNA enzymes in the primordial protein world: in the very synthesis of proteins. Doing so would require RNA to catalyze the formation of the specific bonds, called peptide bonds, that join amino acids in a protein. That, in turn, would imply that RNA could interact chemically with the carbon atoms in amino acids. But so far RNA's ability to make and break bonds has seemed to be confined to the bonds joining phosphorus and oxygen in RNA itself.

Now work by Joe Piccirrilli in Cech's laboratory has shown that an RNA enzyme can break a bond between an amino acid and a nucleic acid, which requires an interaction between the RNA enzyme and the carbon in the amino acid. And if RNA can break such bonds, says Cech, maybe it can make them as well, which would open the possibility of RNA-catalyzed protein synthesis at some point in evolution.

Indeed, RNA-driven protein synthesis may be going on even now, in some present-day ribosomes, according to biochemist Harry Noller of the University of California, Santa Cruz. Within the complex of proteins and RNA that makes up a ribosome, it has been generally assumed that the protein enzymes actually do the catalytic work of forming bonds between amino acids, while the RNA serves as a structural rack for those proteins. But Noller's results suggest the ribosomal RNA may turn out to have the glamour role after all. Remarkably, Noller found that even when he teased away almost all of the protein from the ribosome of a bacterium, the ribosome was still highly effective at assembling amino acids. Noller stresses that he won't know for sure that RNA, and not protein, is actually catalyzing protein synthesis until he can demonstrate that ribosomal RNA completely denuded of proteins is still capable of catalyzing the reaction. But if he succeeds, Noller may have shown that, in one important respect, we are living in an RNA world even today. ■ MICHELLE HOFFMAN