SCIENCE in the INTIFADA

Cutting-edge genetics takes great discipline and skill—Try doing it in a war zone | By Sam Jaffe

No direct road leads from the Mount of Olives to Bethlehem, but even with a few detours, the drive should take about 15 minutes. Yet Moein Kanaan, a geneticist at the University of Bethlehem, leaves his home on the Western slope of the Mount of Olives in Jerusalem by 5:30 in the morning. He usually gets to his lab at Bethlehem University by 9:00.

It takes Kanaan such a long time because, like 8 million other people in Israel and the Palestinian territories, he lives under constant threat of violence. Bethlehem lies over the 1967 border, and Kanaan must pass through as many as half a dozen roadblocks every morning. He usually doesn't have any trouble getting through them, but the delays can be enormous as Israeli soldiers search cars they consider suspicious. The soldiers are looking for bombs and for members of terrorist organizations, not for geneticists. But like all Palestinians, Kanaan must endure the same searches, questions, and nervous glances.

Kanaan's life is far different from what it was three years ago when the Intifada began. Israelis avoid boarding buses and visiting shopping malls for fear of suicide bombers. Palestinians don't know when such an attack might provoke an explosive Israeli response. It's hard enough for a person to merely shop or visit relatives because of Israeli roadblocks. Kanaan and his Israeli collaborator, Karen Avraham, have succeeded in doing the impossible: producing remarkable science in a war zone.

COLLABORATING THROUGH CONFLICT Kanaan's lab has identified several mutations of the connexin 26 gene. Connexin 26 is responsible for more than 30% of all cases of hereditary hearing loss, but exactly why it causes deafness has been a mystery. Kanaan and Avraham have shed light on how it works and what causes it to sometimes malfunction. "Their work has been topical, interesting and cutting edge and surely creative," says Aravinda Chakravarti, director of the McKusick-Nathans Institute of Genetic Medicine at Johns Hopkins University School of Medicine. "I have no doubt that they have advanced the field by their hard work."

The sources of success for Kanaan's lab are also the sources of the conflict going on around him: The Palestinians and the Jews. Both the Palestinian and Jewish populations of the region present fertile ground for genetic research. In the case of the Palestinians, the high consanguinity rate (the marriage of cousins) results in frequent occurrences of recessive traits. Among those traits is deafness, the target of Kanaan's research. The global average for hereditary hearing loss is one out of every 1,000. Among Palestinians the rate is 1.7 out of 1,000; in some Palestinian communities, the rate is as high as 2.5.

Meanwhile, the Jewish population of Israel provides an excellent control group for genetic studies. It comprises dozens of communities from Europe, Asia, and Africa that immigrated and mixed together in Israel during the last century. Therefore, deafness rates among Jews are almost exactly equal to the global average. "It's a perfect laboratory for doing comparative genetics," says Avraham.

It's also a battleground. Since the present Intifada was launched in September 2000, more than 2000 people have been killed and 6000 injured. Another 5000 have been imprisoned. Kanaan himself spent nine months in an Israeli prison for alleged political activities during the first Intifada (which ended in 1993). Now he avoids politics and keeps his activities to science, which he sees as an expression of his political beliefs. "Just by collaborating with Israelis I'm making a political statement," Kanaan says. "Just by bringing visitors to my campus to see the destruction wrought by the occupation, I'm making a political statement."

Indeed, it's hard to miss the bullet scars on walls left unpatched after gun battles early in the Intifada. A wall in the school's library has a hole the size of a watermelon caused by an anti-tank shell that pierced it. Rather than patching the hole, the administration covered it with a sheet of polyurethane as a testament of the violence for future generations. Posters of "martyrs," suicide bombers who killed or injured Israeli civilians, cover campus walls.

Oblivious to all this Kanaan concentrates on his mission. "If nothing else, this work will lead to better testing so that people will be aware of whether they are a carrier for a deafness gene," he says. In addition, he has served as a conduit for international aid agencies that have difficulty reaching deaf Palestinians. Kanaan passes out hearing aids donated by a Canadian non-

Schoolchildren at the Atfaluna School for Deaf Children in Gaza; part of Kanaan's research focus to sign off silence.
profit organization to families who donate samples to his lab or who take hearing tests.

Kanaan's Israeli collaborator, Avraham, sees their work as the foundation for a future cure for deafness. "We want to identify every gene that is responsible for nonsyndrome hearing loss in the Palestinian and Israeli populations and then we want to identify every mutation of those genes," she says. "Once we have that, we'll be able to completely understand the molecular workings of deafness and that's when a cure becomes tenable." That cure might involve genetic therapy. Or it could be a matter of traditional pharmaceuticals once the mechanism of deafness is fully understood.

GENE THERAPY It's long been known that most cases of hereditary deafness result from the loss of hair cells in the inner ear. What actually causes the death of hair cells, however, remains a mystery. In about a third of such cases, the GJB2 gap junction protein (which is encoded by the connexin 26 gene) is to blame. More than 70 connexin 26 mutations have been identified.

But about 150 other genes that contribute to deafness haven't been mapped. Avraham says they will all be cloned and mapped within the next five years, and she says her work with Kanaan will make a major contribution to that effort. "It's remarkable how there's been such an explosion of knowledge," she says.

More than a dozen labs throughout the world, including those at Johns Hopkins in Baltimore, Md., the Institut Pasteur in Paris, and the Boys Town National Research Hospital in Boston, Mass., are also attacking the problem. Science superstars with huge government research grants head some programs. Avraham and Kanaan, whose joint work is funded by the National Institutes of Health, run an operation that pales in comparison to those larger labs. Yet in many instances, the two collaborators have outpaced their competitors, says Mary Claire King of the University of Washington, who collaborates with Avraham and Kanaan in their research. "It's amazing how much they have accomplished with how little they had to start with," King says.

It's even more amazing when one considers the special difficulties of doing research in the region. "I've lost thousands of dollars worth of reagents and instruments when electricity was cut during fighting and the generator failed," Kanaan says. When he wanted to set up an isotope station in his laboratory, his Israeli supplier refused to ship him radioactive products. It took multiple letters to multiple Israeli ministries before he was granted permission. Even with permission, no Israeli delivery company will bring the shipments into Bethlehem, out of fear for the driver's safety. So Kanaan has to pick up the isotopes in Jerusalem and drive them into Bethlehem himself, in a lead-lined box in the back seat.

At one point, a PCR head failed during a blackout and Kanaan carted it into Jerusalem for repairs. The small unit consisted of smooth bore metal with wires and switches coming out of it. Kanaan put it under some blankets in his trunk. Israeli soldiers stopped his car to inspect it for explosives. When they opened the trunk they jumped back and grabbed for their weapons, thinking it was a car bomb. "That took some explaining," says Kanaan, who was eventually allowed to pass through.

Although Avraham's lab is removed from the fighting, she too has encountered security-related difficulties. A Palestinian gradu-