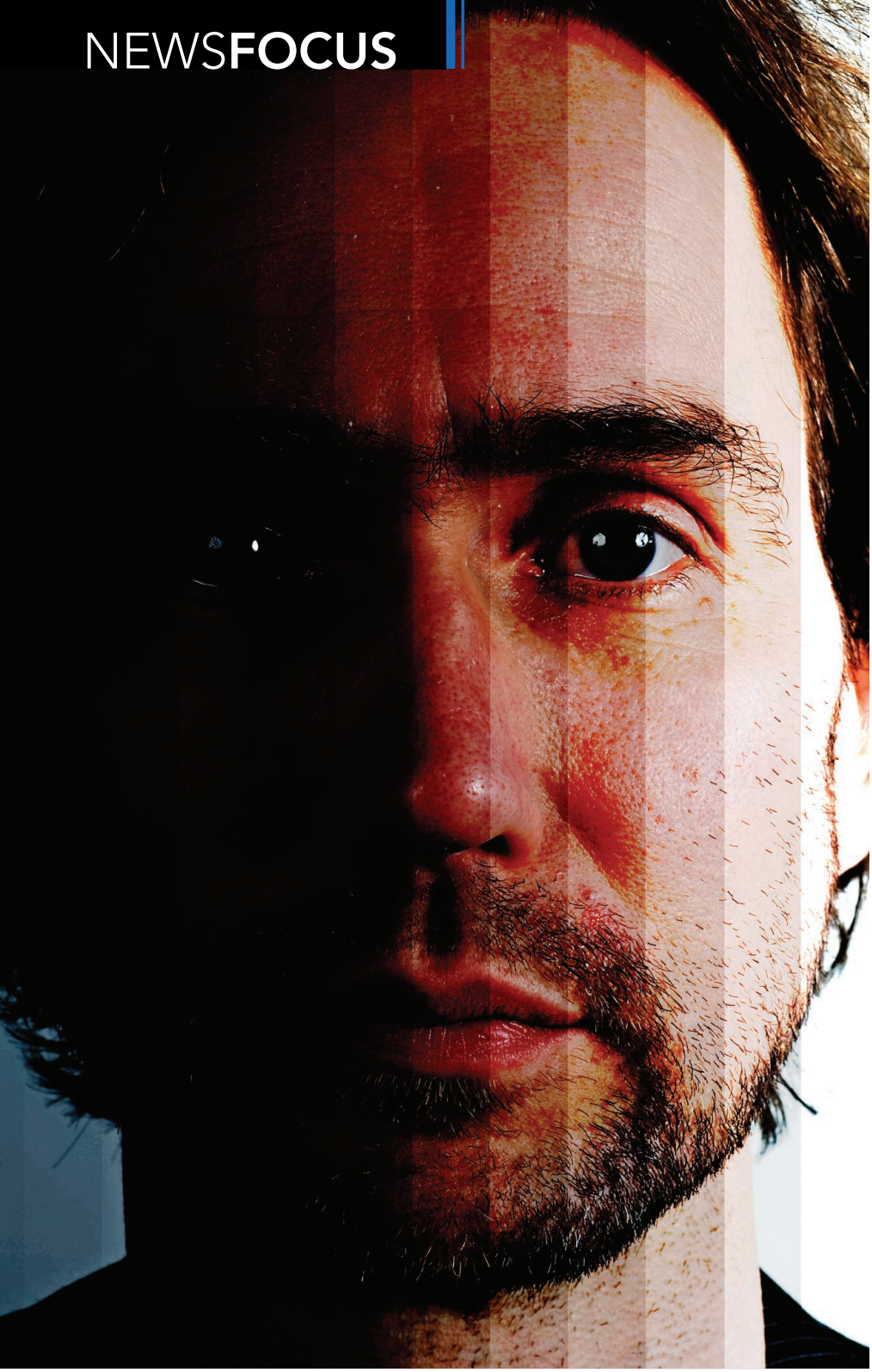

Can This DNA Sleuth Help Catch Criminals?

Forensic geneticist Manfred Kayser is exploring whether DNA found at a crime scene can predict what a suspect looks like

ROTTERDAM, THE NETHERLANDS—The murder was heinous, there were no witnesses, and the police had few clues—except for some skin found under the fingernails of the victim that might belong to the killer. And that was all it took. From a few nanograms of DNA in the skin cells, a police lab determined that the murderer was a man of European origin with brown eyes and straight, dark-brown hair, approximately 45 years old and balding, and likely 1.90 meters in height. Within a few more hours, a police computer spewed out a sketch of the man's face seen from three different angles, which was all over the evening news. Soon, calls started pouring in from people who recognized the suspect.

Sure, that's science fiction. But according to German gene sleuth Manfred Kayser, the scenario might come true one day. Kayser, who leads the forensic molecular biology department at Erasmus University Medical Center here, is at the forefront of an emerging research area that seeks to predict people's looks, age, and geographic ancestry from their DNA. If successful, the endeavor, sped along by the genomic revolution, could provide crime fighters with a powerful new toolbox.

Kayser's group made headlines around the world last year with a paper showing how the DNA in a blood sample can give away someone's age—albeit with a margin of error of at least 9 years. His group has developed a DNA test to predict someone's eye color; work on hair color, skin color, and other traits is in progress. Kayser is "an upcoming star" in forensic DNA phenotyping, as the field is called, says Bruce Budowle, a geneticist with 40 years of experience with the FBI who is now at the University of North Texas Health Science Center in Fort Worth. He's "a clear leader," adds Christopher Phillips, a forensic geneticist at the University of Santiago de Compostela in Spain.

The genetic clues that Kayser and others are trying to glean from minuscule amounts of blood, semen, saliva, and hair are unlikely to be introduced as evidence in a courtroom. After all, when someone is suspected of a crime, or charged, a conventional DNA fingerprinting test can determine if his or her DNA matches traces found at the crime scene. Instead, forensic DNA phenotyping could be useful during an investigation, when predicting a criminal's looks can help the police focus their search.

Forensic DNA phenotyping raises new ethical and legal issues, and the Netherlands is the only country so far to regulate the practice in a new law (see sidebar, p. 840). But Kayser doesn't anticipate that the concerns will stop

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the field. "We are not doing anything else than what police are doing with eyewitnesses," he says. Except for one thing, he asserts: DNA will prove a more reliable witness.

Music and animals

Kayser, 43, isn't fascinated by crime. He doesn't read John Grisham novels or watch *CSI*, the sleek TV hit show centered on forensic research. His lab looks as unexciting as any other molecular biology lab in the world. In fact, Kayser entered the entire field more or less by chance.

He was born and raised in East Berlin in the communist era. As a teenager, he developed passions for both music and the animal world, neither of which were particularly appreciated in the German Democratic Republic, he says. After high school, he worked in the frog collection of the Natural History Museum in Berlin; he was accepted as an accordion student at the Weimar conservatory but eventually chose to study biology at the University of Leipzig in 1989. Two months later, the Berlin Wall came down.

His first experiences with forensic science left him frustrated. Between 1994 and 1998, at Humboldt University in Berlin, Kayser studied microsatellites—short, repetitive DNA sequences—on the human Y chromosome. The work, carried out mostly at the university's Institute of Legal Medicine's genetic research lab, had obvious forensic applications; in rape cases, for instance, evidence often comes from vaginal swabs that contain a mix of DNA from perpetrator and victim. Zooming in on the Y chromosome ensures that you're looking at the rapist's DNA.

Kayser's work helped lay the groundwork for male identification using the Y chromosome, a now widespread method. But Kayser says it took a long time for the technique to become accepted in forensics. "Forensic scientists aren't the most open-minded people when it comes to innovative science," he says. "It was discouraging." He decided to join anthropological geneticist Mark Stoneking's lab at Pennsylvania State University, University Park. Stoneking was piecing together the human history of Polynesia with mitochondrial DNA, which is inherited via the maternal line. Kayser's expertise with the Y chromosome—which tells the male story—complemented this work perfectly, Stoneking says.

Less than a year later, Stoneking moved to the Max Planck Institute for Evolutionary Anthropology in Leipzig. Kayser joined him and stayed in his old college town until he was offered the leadership of a new forensics department at Erasmus University Medical Center in 2004. In an unusual arrangement, his department is co-funded by the Netherlands Forensic Institute (NFI), a governmental lab in The Hague. NFI management recognized that an academic setting would be a more fertile place to invest in science and development than a lab that's loaded with casework, according to Kayser.

"When I saw the business plan, I realized this department was really going to be a unique place," he says, because it would run "the full monty" from basic science to developing and validating tests. Kayser works closely with NFI researchers and with Peter de Knijff, who runs a well-established forensic genetics lab at Leiden University Medical Center where Kayser did part of his Ph.D. work. The three groups have formed a consortium that in 2008 bagged a €6.5 million grant from the Netherlands Organisation for Scientific Research.

Kayser said it was relatively easy to settle in Holland—although he misses sourdough bread and other things German. From his 10th-floor office, he has a view of Rotterdam's ultramodern skyline. And although he would have preferred a city with more historic character, he feels he can't complain: After all, the Germans flattened Rotterdam's ancient center in 1940.

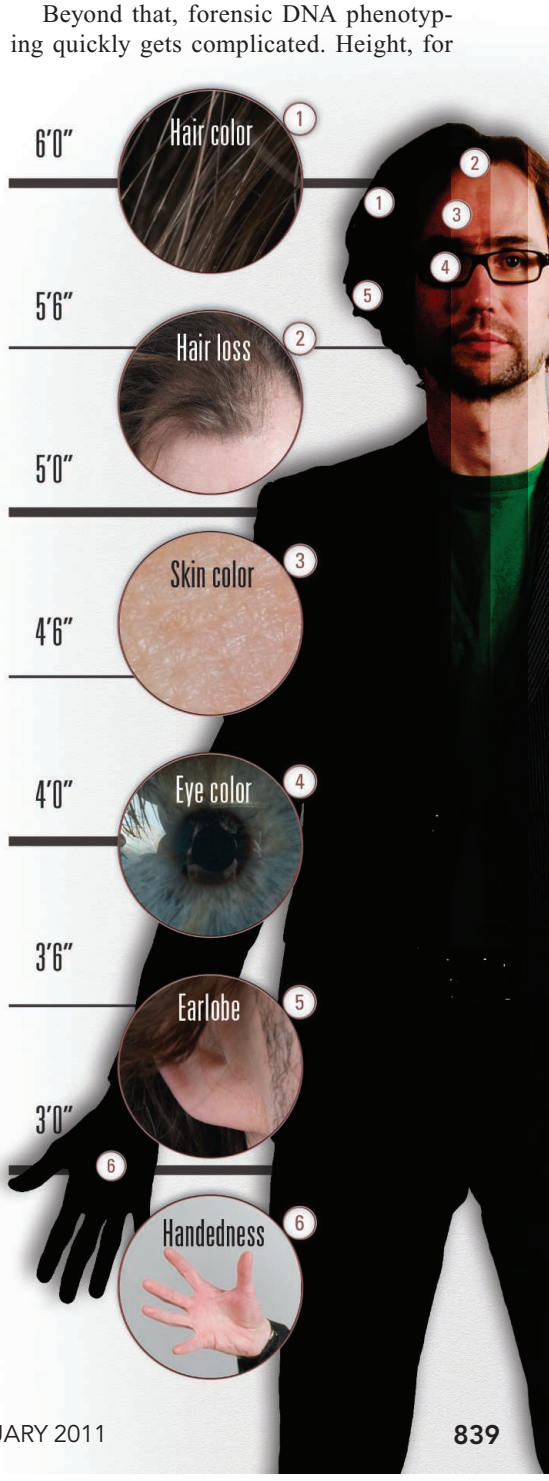
Eyes, hair, and skin

The division of labor within Kayser's 15-person lab reflects the stages within the full monty. Some researchers are primarily focused on finding the genes and genetic markers that underlie phenotypic differences, utilizing so-called genome-wide association studies, for instance. Others are working on turning what's found into actual forensics tests and validating them—a laborious process governed by international standards.

Eye color was low-hanging fruit. Over the past 2 years, his group has developed a test, called Irisplex, based on the identity of just six so-called single-nucleotide polymorphisms. It can now predict with over 90% accuracy whether someone has blue or brown eyes—not perfect, says Kayser, but a lot better than eyewitness testimony, which research has shown to be off the mark at alarming rates.

Last month, Kayser's team published a paper in *Human Genetics* that indicated hair color, too, can be predicted fairly accurately, at roughly 90% for red or black hair and 80% for blond or brown. Those findings are now being translated in a test kit too—most likely combined with eye color, so as to save precious DNA. Skin color is the next candidate. Although his team and others have identified some of the genes involved—they overlap with those for eye and hair color—the picture isn't complete yet.

Beyond that, forensic DNA phenotyping quickly gets complicated. Height, for



Predictable? Many visible traits are at least in part genetically determined and may be predictable from a person's DNA—but the only validated test so far is for eye color.

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instance, is known to have a high degree of heritability: Although diet plays a role in how fast and tall people grow, much of the variation between people is caused by genes. Indeed, a genome-wide association study among 180,000 people published last year revealed more than 180 genetic loci that appear to influence adult height—but together, they account for only 10% of the variation between individuals. De Knijff believes height to be so complex that a useful DNA test is "a bridge too far."

The age test offered a different challenge, as it's not something one can easily read in a person's genome. People have tried to predict age by counting the number of mutations in a person's mitochondria, or measuring the length of their telomeres—the protective caps on the ends of chromosomes, which fray as we age—but both pose practical problems. Kayser's method instead relies on circles of leftover DNA stored in T cells whose amount decreases as people get older.

The field could also target traits like hair structure, baldness, handedness, and earlobe attachment. Its greatest triumph, however, would be that computer-generated, DNA-based facial sketch. Kayser's group is working on it as part of a consortium of labs called VisiGen that Kayser founded with Tim Spector of King's College London. Fan Liu, a genetic epidemiologist in Kayser's lab, is trying to link genome data to key facial morphology traits, such as facial width or nose size. Kayser is cautious about the prospects. "On paper, it's possible," he says. The extreme resemblance between monozygotic twins suggests that facial features are mostly genetic. "But we have no idea yet what genes they are or how complex it is."

Ingrained racism

Kayser's department is also working on tests that can determine someone's biogeographical ancestry. The technique appears to have been used in hundreds of crime investigations in the United States, but modesty is still in order, says Kayser. Although several companies offer detailed ancestry tests to the public, scientists don't have a strong basis to go much beyond the continental level—that is, predicting whether someone is, say, European, sub-Saharan African, East Asian, or Native American. Distinguishing a Norwegian from a Swede, for example, is not usually possible, and Kayser rejects as "totally baseless" a controversial U.K. program to use DNA to determine asylum seekers' nationality (*Science*, 2 October 2009, p. 30).

This application of forensic DNA phenotyping is an area filled with explosive issues about race and crime about which the debate hasn't fully begun. Most forensic DNA phenotyping predictions will likely come with a significant level of uncertainty, as opposed to conventional DNA fingerprinting matches, and police officers may have trouble interpreting them. Moreover, genetic ancestry does not equal race, a concept that most scientists shun because it has no well-defined meaning, and does not necessarily predict someone's appearance. "Ancestry and appearance overlap, but they're not the same," Kayser says.

Just how important caution is was driven home to Kayser by a series of psychology studies, published in 2004, that showed how deeply ingrained stereotypes about black men and crime are among U.S. law enforcement officers. "It was an eye-opener to me," he says. It will be important for scientists like him to explain the uncertainties in DNA-based phenotyping carefully, he stresses.

Fortunately, says Budowle, Kayser is unlikely to oversell his science to overzealous cops. "Manfred knows the molecular biology but also the population genetics and the statistics," he says. "He won't overstate the evidence, and he'll make clear what the limitations are." **–MARTIN ENSERINK**

Emerging Forensics Field May Hit Legal, Ethical Obstacles

A year after a 16-year-old girl was brutally raped and murdered in the Netherlands in 1999, forensic geneticist Peter de Knijff broke the law himself. At the police's request, he set out to determine the geographic ancestry of the murderer from DNA in his semen. That was, he later admitted, "completely illegal" under Dutch law, which at the time allowed using DNA for traditional DNA identification but not for determining race, looks, or disease risk. De Knijff has no remorse. The police were unable to solve the case, and tensions were escalating in the rural community where the girl lived. Many pointed fingers at a nearby hostel for Kurdish, Iraqi, and Afghan asylum seekers. De Knijff's analysis showed that the killer was most likely from northwest Europe, which helped cooler heads prevail.

His dilemma could arise any day in many countries. In the wake of the murder—still unsolved today—the Dutch parliament adopted a law in 2003 regulating forensic DNA phenotyping, the use of DNA samples to predict a suspect's ancestry or physical characteristics (see main text). But the Netherlands is still the only country to have done so.

Countries such as Belgium and Germany—and the U.S. states of Indiana, Rhode Island, and Wyoming—explicitly ban the practice, says Bert-Jaap Koops, a professor at Tilburg University Law School who studies the issue. In the United Kingdom and most U.S. states, forensic DNA pheno-typing isn't explicitly regulated but is allowed under existing laws for forensic DNA. Geographical ancestry tests appear to have been used in several hundred U.S. investigations, says Pamela Sankar, a bioethicist at the University of Pennsylvania. Most were done by a company called DNAPrint Genomics, she says, which ceased operations in 2009.

Sankar, who is tracking the field with funding from the U.S. National Human Genome Research Institute, says forensic DNA phenotyping raises ethical and legal issues that need more debate. Her own research, for instance, suggests that police officers may not realize that—as opposed to the high degree of certainty in DNA fingerprinting—phenotyping is probabilistic in nature. Cops could also use ancestry predictions, however imprecise, as an excuse to target minority populations, she says.

Other dilemmas loom. In theory, knowing that a criminal is, say, a hemophiliac or a diabetic could help nab him. But the 2003 Dutch law categorically bans looking for disease-related genes because it would violate a suspect's privacy and the "right not to know," a basic tenet of medical ethics. (The law allows only the prediction of visible traits and "race.")

Koops argues that these restrictions are overly protective; if genetic sleuthing can reveal that a killer has a very mild or curable disease, or is likely to be a chain smoker, solving the crime might well trump individual rights, he says. The distinction between visible traits and disease is not always tenable anyway, says forensic geneticist Christopher Phillips of the University of Santiago de Compostela in Spain. A mutation in a gene called *MC1R* can cause pale skin, for instance—which increases the risk of melanoma. "Predictive tests should confine themselves to the visible," he says, "but sometimes this encroaches on the private at the same time."

The paradox is that conventional DNA fingerprinting has been introduced with the reassurance that it can never reveal any personal information—but now, it's personal information that forensic geneticists are after. That's why caution is important, says Phillips. "If we move too quickly, the whole edifice of public confidence in DNA profiling could erode." **–M.E.**