changing the DNA codon from CGA to GGA. This changes the complementary mRNA codon from GCU to CCU, which specifies proline. A mutation that changes the amino specified by a codon is known as a **nonsynonymous** (or **replacement**) **substitution**. Switching an amino acid may alter the function of a protein. For example, having a proline versus an alanine as the 49th amino acid in taste receptor TAS2R38 influences a person's ability to taste bitter flavors.

A mutation is any change in sequence in the genome of an organism. Some mutations alter the phenotype; others do not.

Finally, consider a substitution that can occur in the third position of the codon specifying tryptophan. A C-to-T transition changes the DNA codon from ACC to ACT. This changes the mRNA codon from UGG to UGA. UGA is a stop codon. It signals that the protein is complete and no more amino acids should be added. A mutation that introduces a premature stop codon is called a **nonsense mutation**. Nonsense mutations often render the encoded protein nonfunctional (Yamaguchi-Kabata et al. 2008). Many humans carry loss-of-function nonsense mutations in both of their copies of the gene for the muscle protein alpha-actinin-3 (North et al. 1999). The nonsense allele is overrepresented in elite endurance athletes and underrepresented in elite sprint and strength athletes (Niemi and Majamaa 2005; Roth et al. 2008).

Changing the meaning of a codon is not the only way a point mutation can alter protein function or expression. Many genes in eukaryotes contain intervening sequences, or **introns**, embedded among the coding sequences, or **exons**. The introns are transcribed into the mRNA and must be spliced out before translation. Mutations in splice sites can prevent introns from being excised, resulting in production of abnormal proteins. Janna Nousbeck et al. (2011) discovered a splice-site mutation in humans that causes adermatoglyphia—the absence of fingerprints (Figure 5.23). Mutations in the promoter regions of genes, noncoding sequences that play a role in gene regulation, can alter gene expression.

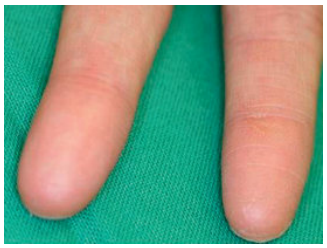

Figure 5.23 Some people lack fingerprints The condition is called adermatoglyphia, and is informally known as immigration delay disease. From Nousbeck et al. (2011).

Like point mutations, insertions and deletions (collectively called **indels**) vary in their effects. And as with point mutations, the genetic code shows why. Insertion or deletion in a coding region of one, two, or any other number of nucleotides not a multiple of three results in a shift of the codon reading frame. This changes the meaning of every codon downstream from the mutation.

The mutational mechanisms we have considered in this section stock populations with a diversity of alleles. In the next few chapters, we will be concerned with the relative frequencies of different alleles in populations. **Computing Consequences 5.2 (next page)** shows how allele frequencies can be quantified.

5.3 Where New Genes Come From

As with mutations that create new alleles, many mechanisms generate new genes (Long et al. 2003; Kaessmann 2010). We cannot cover them all, but we can get a sense of where new genes come from by considering a few examples.

Gene Duplication

Two mechanisms of **gene duplication** are thought to be among the most common sources of new genes. The first is **unequal crossing over**, an error in the genetic recombination that happens during meiosis. In normal crossing over, homologous chromosomes (the maternal and paternal members of a pair) align side by side during prophase of meiosis I and exchange stretches of DNA containing the same loci. In unequal crossing over, the homologous chromosomes align incorrectly. This can happen if the same nucleotide sequence occurs in more than