To confirm and refine the 3C observations, the authors used DNA-FISH (fluorescence in situ hybridization). The observed interchromosomal interactions are largely monoallelic and occur in only a minority of cells (~30 to 40%). As with the 3C technique, the percentage of cells with colocalized alleles was higher in naïve than in differentiated cells, and no colocalization was detected in fibroblasts that do not express the cytokine genes. Because most colocalized genes are not located in heterochromatic regions identified by HP-1 staining, the authors propose that the genes are held in an environment that "poises" them for rapid expression upon stimulation. It would be interesting to test whether this nuclear compartment also holds other genes, such as *Il2*, known to be rapidly expressed by naïve T cells.

The hypothesis of a poised nuclear compartment is not fully borne out by data comparing wild-type and RHS7$^{-/-}$ T cells. The 3C technique gives the expected result: RHS7$^{-/-}$ cells showed decreased interaction of *Ifnγ* with the *Il5* promoter and RHS6 relative to wild-type cells. However, by DNA-FISH, more RHS7$^{-/-}$ than wild-type cells displayed colocalized *Ifnγ* and T$_H$2 cytokine loci (although colocalization was not as "close" in RHS7$^{-/-}$ as in wild-type cells). Consistent with decreased interaction between *Ifnγ* and the T$_H$2 LCR, RHS7 deletion resulted in slower *Ifnγ* transcription without affecting expression kinetics of *Il5* or *Rad50*, which are not controlled by the T$_H$2 LCR. The impairment in *Ifnγ* transcription in RHS7$^{-/-}$ cells could be a nonspecific outcome of introducing a deletion in the T$_H$2 LCR, or it could result indirectly from the known effects of RHS7 on *Il4*, *Il5*, and *Il13*. RHS7 might also have a cis influence on genes such as *Irf1* (also linked to the *Il4* locus) that would then affect *Ifnγ* expression indirectly. Additional studies will be needed to resolve these issues.

T$_H$1 and T$_H$2 cell differentiation are critical for proper immune responses, and imbalances in the function or activity of these cell types are responsible for many immune diseases, including autoimmunity and asthma. Understanding the mechanisms regulating the development and function of these cell types is therefore important from a clinical perspective. Equally interesting is the possibility of using the well-characterized program of T$_H$1/T$_H$2 lineage commitment to unravel the complex interconnections of regulatory networks that control cell differentiation.

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PSYCHOLOGY

Appearance DOES Matter

Leslie A. Zebrowitz and Joann M. Montepare

Take a look at these two snapshots (see the figure). Which man is more babyfaced? Most viewers would say it's the person on the right. And that's the person who lost a 2004 U.S. congressional election to his more mature-faced and competent-looking opponent. In fact, about 70% of recent U.S. Senate races were accurately predicted based on which candidates looked more competent from a quick glance at their faces. This remarkable effect, reported by Todorov *et al.* on page 1623 of this issue, likely reflects differences in "babyfacedness" (*1*). A more babyfaced individual is perceived as less competent than a more mature-faced, but equally attractive, peer of the same age and sex (*2*, *3*). Although we like to believe that we "don't judge a book by its cover," superficial appearance qualities such as babyfacedness profoundly affect human behavior in the blink of an eye (*4*).

What facial qualities make someone look more babyfaced and less competent? Facial measurements and computer modeling reveal that babies and babyfaced adults of 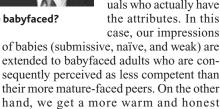all ages share such features as a round face, large eyes, small nose, high forehead, and small chin (*2*, *3*, *5*). So a babyish face is not synonymous with age, which Todorov *et al.* (*1*) eliminated as an explanation for their findings. This general quality also seems to be racially universal and evident in both sexes (*2*, *3*). However, a woman's facial anatomy tends to be more neotenous than a man's, which may be a disadvantage for women when vying for leadership positions (*6*). The association between facial maturity and perceived competence is ubiquitous: Babyfaced individuals within various demographic groups are perceived as less competent, whether by their own or another group. Its impact can be seen even for famous politicians: When

Which person is more babyfaced?

images of former U.S. presidents Reagan and Kennedy were morphed to increase babyfacedness, their perceived dominance, strength, and cunning decreased significantly (*7*).

Why do we think babyfaced people are less competent, at first glimpse? According to the ecological theory of social perception, our ability to detect the attributes of age, health, identity, and emotion has evolutionary and social value. Thus, we have a strong, built-in, predisposition to respond to facial qualities that reveal these characteristics. Moreover, our responses can be overgeneralized to people who look like individuals who actually have the attributes. In this case, our impressions of babies (submissive, naïve, and weak) are extended to babyfaced adults who are consequently perceived as less competent than their more mature-faced peers. On the other hand, we get a more warm and honest impression from a babyface (*2*, *3*, *5*).

So what are the social—even political—consequences of our behavior? One must consider the context. Just as competent-looking, mature-faced individuals are favored as congressional leaders, so are

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they favored for other occupations requiring leadership and intellectual competence. However, those occupations requiring warmth, such as nursing, are most likely assumed by babyfaced adults (*2*, *3*). Contextual effects are also seen in judicial decisions. Judges are more apt to believe denials of negligent acts by mature-faced defendants, whose competent appearance is inconsistent with carelessness. In contrast, they believe denials of intentional transgressions by babyfaced defendants, whose warm and honest appearance is not compatible with such malfeasance (*2*, *3*). Shifts in the popularity of American actresses tell a similar tale regarding contextual relevance of perceived competence. Actresses with mature faces are favored during times of social and economic hardship. But in prosperous times, we turn our preference toward those with a baby's glow (*8*).

When does perceived competence fail to predict election outcomes? Todorov *et al*. found that more competent-looking candidates were defeated in 30% of races. One possible explanation is that face biases could have favored babyfaced candidates in those particular contests. It would be interesting to determine whether babyfaced candidates have the edge in races where polls show that integrity is a highly relevant trait. Like competence, perceived integrity is an important quality used to judge politicians,

and it favors babyfaced individuals (*9*, *10*). The more competent-looking candidates also had only a small advantage in contests between candidates of different sexes. This was attributed to people's reluctance to judge the relative competence of male versus female opponents (*1*). Such concerns should be minimal when judging babyfacedness. Thus, we may better predict outcomes in mixed-sex contests if babyfacedness is used as a proxy for perceived competence.

Are we far from predicting the winner of an election based on voters' responses to a candidate's appearance? Unfortunately, the Todorov *et al*. study shows that this reality may be all too near. The study has important implications for political marketing, social decision-making, and the democratic process. It also highlights unanswered questions about appearance biases at both the neuroscience and social science levels. What brain mechanisms underlie automatic reactions to superficial qualities such as facial appearance? How can we inoculate people against biased reactions to such qualities? The latter question is particularly important given that more competent-looking victors in congressional elections are not likely to be smarter or bolder than babyfaced losers. Indeed, Todorov *et al*. noted that more babyfaced men tend to be slightly more intelligent (*1*). They also tend to be

more highly educated, contrary to impressions of their naïveté, and more assertive and more likely to earn military awards, contrary to impressions of their submissiveness and weakness (*2*, *3*). Understanding the nature and origins of appearance biases has real-world value, not the least of which may be identifying electoral reforms that could increase the likelihood of electing the most qualified leaders rather than those who simply look the part.

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MATERIALS SCIENCE

Snapshots of Crystal Growth

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Crystallization is essential for the manufacture of products as varied as electronic devices, large-tonnage commodity materials, and high-value specialty chemicals such as pharmaceuticals. Yet our understanding of the crystallization process remains limited, especially for organic, polymeric, and protein crystals. Once a crystal has formed, its internal structure can be determined by x-ray diffraction, but unraveling the key steps in its crystallization requires tools that allow control and microscopic visualization of crystal growth, particularly at the early stages that often determine crystal properties such as defect density, purity, size, morphology,

and polymorphism (the ability of a material to adopt different crystal structures).

Several research groups have used atomic force microscopy (AFM) (*1*) to achieve a comprehensive understanding of crystal nucleation and growth at microscopic length scales, building on early studies that established the capability of this technique for examining crystal surfaces and crystallization (*2–5*). The use of AFM for crystallization studies involves scanning a small tip (often made from silicon or silicon nitride) over a crystal surface immersed in the crystallization medium. This approach reveals the two-dimensional lattice structure of the exposed crystal surfaces and permits direct visualization of surface features (such as terraces, ledges, and kinks) to which incoming molecules attach.

In situ AFM imaging of this kind is particularly well suited to small-molecule or protein crystals, which are inherently soft and easily damaged when studied in air or a

vacuum. In liquid media, these materials are less susceptible to mechanical damage by the scanning tip, because the forces between the tip and the sample are smaller than they would be in air or vacuum (*6*). Moreover, a liquid medium precludes capillary condensation between the tip and the sample, which would otherwise create meniscus forces that can damage soft surfaces during imaging. Combined with the real-time imaging capability of AFM, the weaker tip-sample forces in liquids enable reliable real-time visualization of crystal growth in situ (*7*).

In a typical AFM study of crystal growth, a pregrown crystal is affixed to an AFM sample stage or is crystallized on a surface exposed in the AFM cell. Crystal growth is then prompted by a change in concentration or temperature. For example, the growth of crystalline organic conductors can be regulated precisely through adjusting the electrochemical potential, which governs the solute concentration at the crystal interfaces (*4*, *8*).

AFM has proven especially useful for examining the crystallization of proteins, including lysozyme (*2*), canavalin (*9*), hemoglobin (*10*), and insulin (*11*). Most insulin crystals (see the figure, A) consist

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