Response to *The Intriguing Story of Jews' Resistance to Tuberculosis*, written by Martini M, Mahroum N, Bragazzi NL, Parodi A.

To the Editor

Regarding the article, *The Intriguing Story of Jews' Resistance to Tuberculosis* [1], it is indeed intriguing that Jews were blamed for all aspects of diseases, from causing them, to spreading them, or alternatively, to being resistant to them.

In the Middle Ages, Jews were blamed for causing the Plague (Black Death) epidemics, even though the Pontiff Clement VI stated that Jews were also dying from the Plague, and hence could not be the cause of it.

In the early decades of the 20th century, Jews were blamed for spreading the influenza pandemic, although even my grandparents became ill from it.

The assumed Jewish resistance to tuberculosis (TB), as described in detail in the comprehensive study by Martini and colleagues, was contradicted by the hideous Nazi experiments on Jewish children in Neuengamme Concentration Camp, near Hamburg, Germany. In 1945, Jewish inferiority was stated to be due to lack of resistance to TB, as described in the catalogue accompanying the exhibition "Nazi medicine," presented by the Sydney (Australia) Jewish Museum in 2008.

It was mathematically calculated that the Jewish prisoners interned in the Lodz Ghetto [2] either died due to hunger or to the outrageous living conditions, and that within 2 months or so, all of the inhabitants would have died from the TB epidemic, making the gassing unnecessary.

Today, there is some evidence of racial resistance to some diseases, and some illnesses are thought to be environmentally determined, with pre-existent health input.

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References

1. Martini M, Mahroum N, Bragazzi NL, Parodi A. The Intriguing Story of Jews' Resistance to Tuberculosis, 1850–1920. *IMAJ* 2019; 21 (3): 222-8.
2. Weisz GM, Albury WR. Ghetto medicine: the special case of Ghetto Lodz, 1940–44. *IMAJ* 2013; 15 (4): 137-42.

Capsule

Association of BCG vaccination in childhood with subsequent cancer diagnoses a 60-year follow-up of a clinical trial

The Bacillus Calmette–Guérin (BCG) vaccine is currently the only approved tuberculosis vaccine and is widely administered worldwide, usually during infancy. Previous studies found increased rates of lymphoma and leukemia in BCG-vaccinated populations. **Usher** and colleagues examined whether BCG vaccination was associated with cancer rates in a secondary analysis of a BCG vaccine trial. Retrospective review (60-year follow-up) of a clinical trial in which participants were assigned to the vaccine group by systematic stratification by school district, age, and sex, then randomized by alternation. The original study was conducted at nine sites in five U.S. states between December 1935 and December 1998. Participants were 2963 American Indian and Alaska Native schoolchildren younger than 20 years of age with no evidence of previous tuberculosis infection. Statistical analysis was conducted between August 2018 and July 2019. A total of 2963 participants, including 1540 in the BCG vaccine group and 1423 in the placebo group, remained after exclusions. Vaccination occurred at a median (interquartile range) age of 8 years (5–11); 805 participants (52%) in the BCG group and 710 (50%) in the placebo group were female. At the time of follow-up, 97 participants (7%) in the placebo group and 106 participants (7%) in the BCG vaccine group could not be located. Total mortality was 633 participants (44%) in the placebo group and 632 participants (41%) in the BCG group. The overall rate of cancer diagnosis was not significantly different in BCG vaccine vs. placebo recipients (hazard ratio 0.82, 95% confidence interval [95%CI] 0.66–1.02), including for lymphoma and leukemia. The rate of lung cancer was significantly lower in BCG vs placebo recipients (18.2 vs. 45.4 cases per 100,000 person-years; hazard ratio 0.38, 95%CI 0.20–0.74; P = 0.005), controlling for sex, region, alcohol overuse, smoking, and tuberculosis. The authors conclude that childhood BCG vaccination was associated with a lower risk of lung cancer development in American Indian and Alaska Native populations. This finding has potentially important health implications given the high mortality rate associated with lung cancer and the availability of low-cost BCG vaccines.

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Eitan Israeli

"Whoso neglects learning in his youth, loses the past and is dead for the future"

Euripides (ca. 480 BC–406 BCE), Greek playright

"There is no foreign land; it is the traveler only that is foreign"

Robert Louis Stevenson (1850–1894), novelist, essayist, and poet

Capsule

Superantigens spur IgA secretion

Mucosal immunoglobulin A (IgA) is abundant and interacts with the gut microbiome. To examine microbial induction of IgA in humans, **Bunker** and co-authors screened microbiota from infants against mouse and human IgA. A subset of samples bound IgA in a way that indicated the presence of superantigens, which bind T cell receptors or B cell receptors outside of the typical antigen-binding region, leading to nonspecific activation. Putative superantigens in commensal members of Lachnospiraceae-activated human VH3-positive B cells and induced IgA production in mice. The authors suggested that commensal superantigens may be dominant forces behind IgA production in humans.

Sci Transl Med 2019; 11: eaau9356

Eitan Israeli

Capsule

Empowering NK cells against cancer

Tumors release factors, such as the cytokine transforming growth factor-β (TGF-β), that block antitumor immunity mediated by natural killer (NK) immune cells by promoting their differentiation into a less suppressive cell type. **Rautela** and colleagues found that activin-A, another member of the TGF-β family, had similar effects on both mouse and human NK cells but through a pathway independent of TGF-β. Inhibition of activin-A reduced skin cancer growth in a mouse melanoma model, suggesting that targeting this pathway could enhance NK cell function and antitumor immunity.

Sci Signal 2019; 12: eaat7527

Eitan Israeli

Capsule

Targeting parasite's protein kinase

Malaria elimination goals are constantly eroded by the challenge of emerging drug and insecticide resistance. **Alam** et al. investigated how drug targets, such as CLK protein kinases involved in regulation of RNA splicing, inhibition of the parasite's enzymes blocks completion of its complex life cycle. They identified an inhibitor of the parasite's CLK protein kinase that was 100-fold less active against the most closely related human protein kinase and effective at clearing rodent malaria parasites. Not only does this compound halt the development of sexual stages but it also limits transmission to the mosquito vector of the parasite, a key requirement for malaria drugs.

Science 2019;365:eaau1682

Eitan Israeli

Capsule

Resurrecting sentinels in the skin

Langerhans cells are resident innate immune cells in the skin that play essential roles in promoting local immune responses and maintaining skin homeostasis. Langerhans cells arise from fetal progenitors that seed the skin early in development. In a mouse hematopoietic stem cell transplant model, **Ferrer** and colleagues found that monocytes from the blood infiltrate the skin and eventually replenish the Langerhans cell network. These observations are in agreement with previous studies looking at other sites, but the process by which monocytes give rise to Langerhans cells is inefficient, limiting the extent to which they can be renewed in the skin.

Sci Immunol 2019; 4: eaax8704

Eitan Israeli

"After you understand about the sun and the stars and the rotation of the earth, you may still miss the radiance of the sunset"

Alfred North Whitehead (1861–1947), English mathematician and philosopher; best known as the defining figure of the philosophical school known as process philosophy