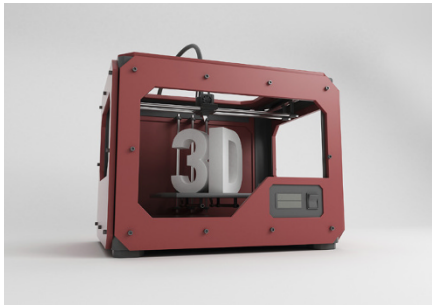
3D bioprinting of human-scale tissues

The ability to engineer tissues in the lab for clinical purposes would provide important relief for the high demands and scarce supply of tissues and organs that are needed for life-saving transplantations. Additionally, engineered tissue from patient derived stem cells would potentially decrease the need to develop and use of animal models for xenotransplantation.

Three-dimensional (3D) printing technology using cell-laden hydrogels is a promising avenue of tissue engineering for human transplantations; however, certain technological constraints have limited the complexity and integrity of tissues built using 3D printing. Because soft and delicate materials are used to print tissues, it can be difficult to achieve enough structural support to create complex and thick shapes necessary to reproduce tissues and organs that are suitable for transplantation. A team at Wake Forest Institute for Regenerative Medicine (Winston-Salem, NC), led by Anthony Atala, has introduced a novel method that significantly improves



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the process of 3D bioprinting, enabling the creation of sturdy, complex, human-scale tissues that are suitable for *in vivo* implantation (*Nat. Biotechnol.* **34**, 312–319; 2016).

To overcome the limitations of structural integrity that are presently associated with 3D bioprinting, the research team developed a unique system that prints a sacrificial scaffold of synthetic biodegradable polymers alongside cell-laden hydrogels. To increase survival of the printed tissues, layers of polymers and hydrogels are printed with a lattice of microchannel pores that allow for vascularization and the easy flow of nutrients and oxygen into the cells. The researchers used computer tomography and magnetic resonance imaging to create digital images of real tissues, which served as shape-templates for the 3D bioprinter.

To test their newly designed bioprinting method, the researchers printed human ear-shaped cartilage, rat calvarial bone and mouse skeletal muscle. In all three experiments, the tissues maintained good structural integrity and the cells constituting the printed tissues were healthy and viable. Importantly, the printed tissues remained healthy after *in vivo* implantation into rats or mice and showed signs of vascularization and incorporation with the surrounding tissues.

This novel method of 3D bioprinting creates new opportunities for producing human-scale tissues and organs for clinical use. Because the cells used for bioprinting can originate from the stem cells of patients themselves, this method could also sidestep many of the problems that lead to transplant rejections.

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TICKS REQUIRE A SQUARE MEAL FOR VIABLE OFFSPRING

As any outdoor hobbyist or pet owner is keenly aware, ticks are a major concern that accompanies warmer weather, when they emerge to feed, mature and reproduce. Ticks pose a specific threat to human health because, while feeding, they can transfer bacteria, viruses and protozoa into host animals. At present, ticks are known vectors for at least 16 zoonotic diseases.

Whereas some parasitic animals supplement their diets with blood, these ectoparasitic arachnids are obligate hematophages, which means that they require blood to survive and mature. Hematophagia poses special challenges, however, to the physiology of blood suckers. Blood contains many essential nutrients that are necessary for various biological processes, bound up in hemoproteins, like hemoglobin; but heme, the important iron-binding component of these hemoproteins, is also cytotoxic, and all organisms must maintain intracellular heme at consistent, low and safe levels.

To maintain this delicate balance, most organisms have metabolic pathways that can synthesize heme as needed and digest hemoproteins when levels rise too high. Curiously however, ticks do not have these pathways. Unlike other hematophages, ticks cannot biosynthesize heme, and all ticks and mites are unable to break down heme into bioavailable iron. This presented a mystery as to how ticks use the heme from their blood meals, which can range in size up to 100 times a tick's bodyweight. To study this question, Jan Perner (University of South Bohemia, Czech Republic) and colleagues fed ticks experimental meals to understand how the presence or absence of heme affects tick metabolism and development (*eLife* **5**, e12318; 2016).

Using an *in vitro* membrane feeding system, Perner's team fed hard ticks (*Ixodes ricinus*) different meals including whole blood, serum that lacked hemoglobin or serum in which hemoglobin had been rescued with artificial supplements. Ticks that consumed a whole-blood meal produced normal eggs that hatched normal larvae whereas ticks that received serum without hemoglobin laid colorless eggs that failed to hatch. However, ticks that received serum with supplements of pure bovine hemoglobin produced normal eggs with healthy embryos. Upon examining the eggs and adult tissues of each group, Perner *et al*. found no apparent differences; only embryo development seemed to depend critically on heme from the blood meal. The researchers suspect that this developmental dependence likely arose as an adaptation to the tick's parasitic lifecycle, and they propose that it is a promising target for future anti-tick interventions.

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