

an ancestral protein related to components of the BAM or TAM systems in the ancestral bacterium that gave rise to the chloroplast.

Chen and colleagues demonstrate that TIC236 is related to TamB, which aids protein transport⁹ between bacterial membrane proteins that form a secretion system (called Sec), located on the inner membrane, and BAM or TAM components in the outer membrane (Fig. 1b). It therefore seems that a mechanism for coupling inner- and outer-membrane transport in chloroplasts has been evolutionarily conserved from an ancestral bacterial system.

However, despite this conservation, the chloroplast protein-import system has evolved to function in the reverse direction relative to the direction of transport in the bacterial export system⁵. The BAM and TAM complexes facilitate export of bacterial proteins from the

cytoplasm to the outer membrane, whereas the TOC and TIC complexes import proteins from outside the chloroplast to inside it. This remarkable reversal of the direction of protein transport probably resulted from the gain of other TOC or TIC proteins that evolved from host-encoded genes to adapt the complexes for the purposes of protein import. These include TOC and TIC receptors and molecular motor proteins known to facilitate transport into the chloroplast³.

Chen and colleagues' results provide convincing evidence for the origin of key elements of the chloroplast protein-import system from an ancestral bacterial protein-export system. Their insights also reveal the adaptation and consequent reversal of an existing protein-targeting pathway that was essential for the ancestral bacteria to successfully take up residence in a host cell, thereby

enabling the host to take advantage of its guest's photosynthetic and metabolic capabilities. ■

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greater masses than their counterparts in the first family. And the third comprises the top quark, the bottom quark, the tau and the tau neutrino, where the charged fermions are even more massive.

After their discovery of the Higgs boson^{1,2}, one objective of the ATLAS and CMS collaborations was to probe the particle's properties, such as its couplings to fermions — the strength of its interactions with fermions. In the current papers, the collaborations combined all the data that they recorded between 2011 and 2017, and each claims to have observed the decay of the Higgs boson to bottom quarks.

In both sets of data, the decay signal is larger than the background, which arises from other particle-physics processes. The statistical significance of the signal is 5.4 and 5.6 standard deviations for the ATLAS and CMS experiments, respectively — well above the conventional threshold of 5 standard deviations needed to claim observation. In addition, the overall yields of the decay are in agreement with standard-model predictions within an experimental uncertainty of roughly 20%.

The Higgs boson decays almost immediately after it is produced. The probability that a particular decay will occur depends on the

PARTICLE PHYSICS

Long-sought decay of the Higgs boson seen

Measurements of the strength of interactions between the Higgs boson and other particles test the current model of particle physics. A key part of this model has been confirmed by observing the most common decay of the Higgs boson.

BORIS TUCHMING

In 2012, the famous Higgs boson was discovered by the ATLAS and CMS collaborations in proton–proton collisions at the Large Hadron Collider (LHC) at CERN near Geneva, Switzerland^{1,2}. Now, writing in *Physics Letters B*³ and *Physical Review Letters*⁴, the two collaborations report the observation of the Higgs boson decaying to a pair of elementary particles known as bottom quarks. This milestone in particle physics confirms the role of the Higgs field — the quantum field associated with the Higgs boson — in providing particles of matter with mass.

When the standard model of particle physics emerged in the 1960s, the main goal of the ad hoc Higgs field was to explain the masses of the weak vector bosons — the force carriers of the weak nuclear interaction. Mathematical consistency required the force carriers to be massless, whereas the extremely short range of the weak interaction was a signature of massive particles. The Higgs mechanism^{5–8} addressed this issue: the masses of the weak vector bosons are not intrinsic, but are the outcome of interactions between these particles and the all-pervasive Higgs field. It was quickly realized that elementary particles of matter called fermions could also get their masses from interactions with the Higgs field^{9,10}.

Several decades later, twelve elementary fermions are known and are arranged in three families. The first family comprises three charged particles — the up quark, the down quark and the electron — and a neutral particle called the electron neutrino. These fermions are the basic ingredients of ordinary matter: the up and down quarks are the constituents of protons and neutrons, and electron neutrinos are emitted from certain radioactive decays.

For a reason that is not yet fully understood, two replicas of the first family exist. The second family consists of the charm quark, the strange quark, the muon and the muon neutrino, where the charged fermions have

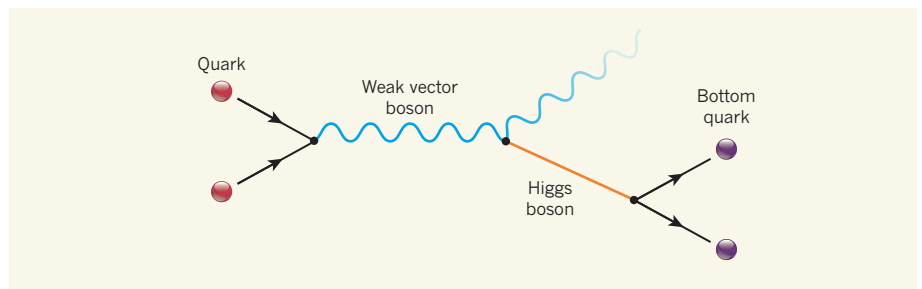


Figure 1 | Production of the Higgs boson together with a weak vector boson. The ATLAS³ and CMS⁴ collaborations report evidence that a particle known as the Higgs boson can decay to pairs of elementary particles called bottom quarks. To detect this decay, the collaborations looked for a particular process in which two quarks arising from colliding protons fuse to form a weak vector boson — a force carrier of the weak nuclear interaction. The weak vector boson emits a Higgs boson that decays to bottom quarks.

couplings to the Higgs boson, which are determined by the masses of the decay products. Because bottom quarks are among the heaviest fermions, the decay to these particles is the most common, occurring about 58% of the time. But even though this decay is dominant, in proton–proton collisions the signal is overwhelmed by the background of bottom quarks produced by the strong nuclear interaction. For this reason, the discovery of the Higgs boson in 2012 involved decays only to vector bosons: photons from the electromagnetic interaction and weak vector bosons from the weak interaction.

To observe the decay to bottom quarks, the two collaborations had to look for subdominant modes of Higgs–boson production, such as the production of the Higgs boson together with a weak vector boson (Fig. 1). A deep understanding of the responses of the particle detector, and sophisticated data-analysis methods that included machine learning, were needed to precisely reconstruct the energies and momenta of the weak vector bosons, tag the jets of particles arising from the bottom quarks, model all the backgrounds and separate these backgrounds from the signal.

The findings are not entirely surprising, for at least two reasons. First, there have been several pieces of evidence for the decay of the Higgs boson to bottom quarks in the past. In 2012, a signal at the level of 2.8 standard deviations was claimed by scientists at the Tevatron proton–antiproton collider, located near Chicago¹¹. Between 2012 and 2018, the ATLAS and CMS collaborations regularly reported outcomes of their search for the decay. In their latest papers before the current work, they obtained evidence at the level of 3.6 and 3.8 standard deviations, respectively^{12,13}. These different pieces of evidence could be considered as a combined observation of the decay.

Second, many other experimental results at the LHC are constraining what could actually be observed regarding this decay. For example, if the Higgs boson had behaved as in the standard model, but had had zero coupling to bottom quarks, the yields of all the other decay modes would be enhanced by a factor of about 2.4, which is contradicted by the data. Considering the overall picture, unless there exist unexpected cancelling effects, the allowed deviations from the standard model are at the level of a few per cent — below the current 20% sensitivity of experiments at the LHC.

Nevertheless, the current results are a great achievement and constitute a major milestone in particle physics. Together with observations earlier this year of the Higgs boson decaying to tau particles¹⁴ and the production of the Higgs boson together with top quarks^{15,16}, the findings directly establish interactions between the Higgs boson and the third family of fermions, therefore pointing to the Higgs field as the origin of fermion masses.

The results are the starting point of an era of precision measurement for the couplings of the Higgs boson to fermions. With more data from the LHC — in particular, after upgrades to the beam intensity in a few years — an accuracy of a few per cent in the measurements should be obtained. This would open the possibility of finding deviations from the standard model and of, for example, uncovering currently unknown particles.

Another milestone would be observing the couplings of the Higgs boson to the second family of fermions. The decay of the Higgs boson to a pair of muons is within the reach of the future upgraded LHC. However, because of the extremely high background in proton–proton collisions, the decay to charm quarks could probably be demonstrated only by using a giant electron–positron collider, which is yet to be constructed. The Higgs boson is therefore far from having revealed all of its secrets. ■

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METABOLISM

Reducing oxygen consumption in fat

Low oxygen levels are a hallmark of expanding fat tissue in obesity, and can lead to type 2 diabetes. In addition to a lack of adequate blood supply, increased oxygen demand in fat cells now emerges as being key to this harmful state.

NOLWENN JOFFIN & PHILIPP E. SCHERER

A major cause of type 2 diabetes is obesity, in which fat cells expand rapidly, in both size and number, and their oxygen demand outstrips supply. This low-oxygen state, known as hypoxia, leads to upregulation of the anti-hypoxic protein HIF-1 α , which in turn causes tissue inflammation and prevents fat cells (adipocytes) from responding normally to insulin^{1,2}. Hypoxia in expanding fat is often thought of mainly as a problem of supply, caused by the inability of blood vessels that deliver oxygen to grow as fast as the surrounding tissue^{3,4}. Writing in *Nature Metabolism*, Seo *et al.*⁵ highlight a pathway by which excessive oxygen consumption in adipocytes can also contribute to hypoxia in expanding fat tissue. This pathway involves the enhanced activity of the enzyme adenine nucleotide translocase 2 (ANT2) in energy-generating organelles called mitochondria.

During normal mitochondrial respiration, electrons are transferred between a series of molecules, and this transfer is coupled to the

removal of hydrogen ions (H⁺, also known as protons) from the central matrix of the mitochondrion into the space between its outer and inner membranes. This process creates a proton gradient that drives the production of energy-carrying ATP molecules in mitochondria by the enzyme ATP synthase. But the process can become uncoupled if protons leak across the inner mitochondrial membrane. Uncoupled respiration results in inefficient ATP production, and thereby increases the intracellular demand for oxygen for further respiration.

High levels of uncoupled respiration can alter cellular physiology, and inhibiting uncoupled respiration with various compounds increases cellular oxygen levels, decreasing hypoxia and so reducing HIF-1 α levels⁶. Any manipulation that leads to a decrease in cellular HIF-1 α activity in fat is metabolically beneficial¹. Thus, a better understanding of uncoupled respiration and how to manipulate it is desirable.

Previous work⁷ by the group that carried out the current study has shown that the rate of