Kaytee Bio, Co. & Ltd.

www.kayteebio.com

KAYTEE BIO
ケイティーバイオ

Personalizing medicine in autoimmune disease

Kaytee Bio is focusing on mechanisms to identify diagnostics and treatments for rheumatoid arthritis.

Some exciting breakthroughs have been made in the treatment of autoimmune diseases through the development and use of targeted and specialized biologic therapeutics. However, there are still areas of unmet need, which Japan-based biotech Kaytee Bio aims to address through the development and commercialization of accurate diagnostics and innovative therapeutics.

Biologics can make major differences to the lives of patients with autoimmune diseases, slowing or halting disease progression, or even reversing it. However, not all patients respond to the drugs; for example, around one-third of rheumatoid arthritis patients show no benefit from individual biologics, so their physicians have to stop treatment and prescribe different therapeutics until they find the one that works for them. This leads to delays in pain reduction and potential worsening of disease. It also has an impact on costs to both the healthcare system and society, as patients lose time at work, physicians and healthcare professionals are involved in repeated appointments to prescribe alternative treatments, and very costly drugs are wasted because they are deemed ineffective for that patient.

Kaytee Bio, which was founded in 2010, is developing a diagnostic for use in detecting early-stage rheumatoid arthritis that tests for an abnormal form of the cytoskeletal protein talin. This protein is involved in cell signaling and cell migration and is normally cleaved by the protease calpain. In rheumatoid arthritis, the protein is cleaved by another enzyme, talin protease, creating a shortened and potentially inflammatory form known as short-talin. Most people with rheumatoid arthritis express higher than normal levels of this shortened version in their blood plasma and peripheral blood mononuclear cells. This finding has allowed Kaytee Bio to create a very specific and sensitive diagnostic for rheumatoid arthritis. Patients who go into remission after successful treatment have normal levels of short-talin, meaning that the diagnostic can also be used to track their response to treatment. Its greater sensitivity compared with tests based on anti-CCP and rheumatoid factor should allow earlier diagnosis, helping patients to begin treatment before the disease damages their joints. Kaytee Bio is seeking partners to help it develop its talin test, both for human use and for the diagnosis of canine rheumatoid arthritis and canine idiopathic polyarthritis by veterinarians.

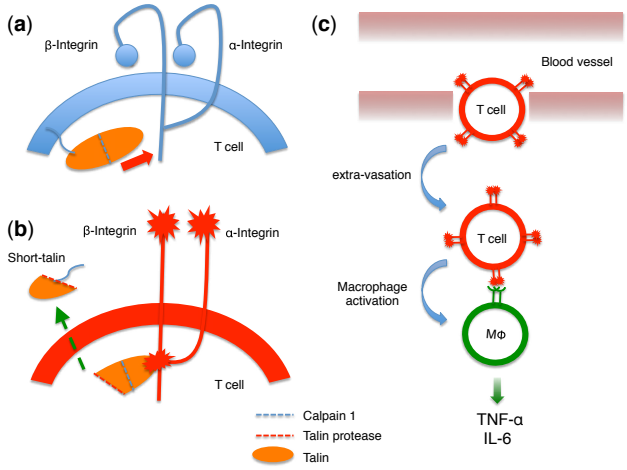

Figure 1: The mechanism of cytokine up-regulation through constitutional activation of integrin by short-talin. (a) Integrins should normally be activated in T cells if talin binds to the cytoplasmic tail of integrin when needed. (b) In patients with rheumatoid arthritis, integrins in T cells should be constitutionally activated by the short-formed talin that is cleaved by the talin protease. (c) Constitutional activation of integrins could lead to the extravasation of T cells, macrophage (Mφ) activation, cytokine production, and bone destruction.

Using another approach, Kaytee Bio has created BiologicMate, a tool that predicts response to biologic therapeutics in patients with rheumatoid arthritis by measuring levels of the peptidase ADAMTS5 (a disintegrin and metalloproteinase with thrombospondin motifs), which has a role in aggrecan degradation in cartilage. Different levels of *ADAMTS5* mRNA can predict the efficacy of each of five biologic therapeutics (etanercept, infliximab, adalimumab, tocilizumab and abatacept). BiologicMate has been launched as 'research use only' test. Kaytee Bio is also developing the tool as an *in vitro* diagnostic (IVD) that could be used to help physicians select the drug that is most likely to be effective, therefore personalizing treatment for individual patients. The company is seeking collaborations to support IVD development.

Kaytee Bio is also working in osteoarthritis, which results from wear and tear of joints. This form of arthritis is most commonly seen in older people, and the number of affected individuals will rise as the global population ages and people live longer and increasingly active lives. Kaytee Bio has developed a test for the enzyme aggrecanase, which breaks down aggrecan in cartilage. This test has the potential to diagnose the disease and predict its prognosis, helping doctors to plan treatment and patient support. Kaytee Bio is open to discussion with potential partners for this project.

In addition to developing diagnostics, Kaytee Bio has therapeutics in its pipeline. Short-talin has been linked with inflammation and bone damage in rheumatoid arthritis caused by integrin activation, T cell migration, synoviocyte activation and cytokine production (**Fig. 1**). Regulation of short-talin could have a role in stopping the sequence and therefore controlling or slowing the progression of this painful and disabling disease. Kaytee Bio is in early-stage development of a series of small-molecule short-talin proteinase inhibitors. All of the company's technology, both diagnostic and therapeutic, is covered by a network of global patents (**Fig. 2**).

Kaytee Bio currently has four employees. With the company now in its sixth year, president and CEO Kensei Tsuzaka is looking to grow the business as its pipeline expands and products advance. To support this, Tsuzaka is seeking investors in the company, as well as R&D partners for its projects.

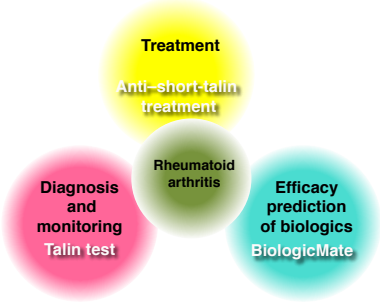

Figure 2: Kaytee Bio has three rheumatoid arthritis projects. The first is the efficacy prediction of biologics using BiologicMate, the second is diagnosis and monitoring using the talin test, and the third is treatment using anti–short-talin therapeutics.

contact
Kensei Tsuzaka, President and CEO
Kaytee Bio, Co. & Ltd.
Funabashi, Japan
Tel: +81 47 411 0017
Email: kayteebio@kd6.so-net.ne.jp