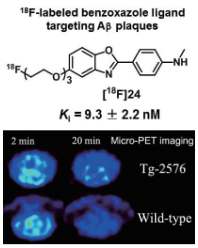
Molecular Imaging of β-Amyloid Plaques for Early Diagnosis of Alzheimer's Disease

New PET Probes for In Vivo Imaging of β-Amyloid Plaques in Alzheimer's Disease

Associate Professor Masahiro Ono, Graduate School of Pharmaceutical Sciences
Professor Hideo Saji, Graduate School of Pharmaceutical Sciences



Alzheimer disease (AD) is the most common form of dementia. The pathological hallmarks of AD are extracellular deposits of β-amyloid (Aβ) plaques and intracellular neurofibrillary tangles. According to the amyloid cascade hypothesis, amyloid deposits constitute a central and initial event in the pathogenesis of AD. Therefore, a tracer agent for positron emission tomography (PET) which specifically binds to these Aβ plaques, will provide an important tool for the non-invasive in vivo diagnosis of AD. Furthermore, it might also be used to predict the development of AD before the onset of dementia and to assess the effect of anti-amyloid therapy. In our recent studies, we showed that [^{18}F]**24**, a novel radiofluoro-pegylated phenylbenzoxazole derivative, has several favorable properties: high affinity for Aβ aggregates (Ki = 9.3 nM); easily labeled with ^{18}F for imaging; good initial brain uptake and fast washout; lower non-specific binding in white matter as demonstrated by autoradiography in vitro and ex vivo using postmortem AD brain sections and Tg2576 mice. These findings suggest that [^{18}F]**24** should be investigated further as a potential PET tracer for imaging Aβ plaques in living brain tissue [fig].

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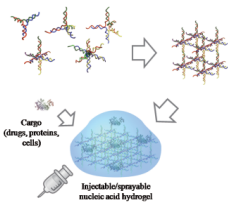
Self-Gelling Nucleic Acids with Injectable, Biodegradable, and Immunomodulatory Functions

Injectable/Sprayable Nucleic Acid Hydrogel as Biodegradable and Biocompatible Drug Delivery System

Associate Professor Makiya Nishikawa, Graduate School of Pharmaceutical Sciences
Professor Yoshinobu Takakura, Graduate School of Pharmaceutical Sciences
Assistant Professor Yuki Takahashi, Graduate School of Pharmaceutical Sciences



Nucleic acids, DNA and RNA, can be used for the construction of nano- to macro-scale DNA/RNA assemblies. Associate Prof. Makiya Nishikawa and his colleagues have developed self-gelling nucleic acids, which gelate under physiological conditions without the use of DNA ligase or any other crosslinking agents. A monomer unit consists of two or more oligonucleotides, each of which has two parts:one being complementary to other strands in the same unit and one (an adhesive end) complementary to the other units. This monomer unit, which is called a polypod-like structured nucleic acid, or polypodna, forms hydrogel through hybridization of the adhesive ends. Any cargo can be incorporated into and sustainedly released from the hydrogels. Immunostimulatory, immunosuppressive or immunomodulatory hydrogels can be prepared by selecting the sequences of the components. Thus, this system can be used for preparing injectable or sprayable nucleic acid hydrogels, which can become biodegradable and biocompatible drug delivery systems.

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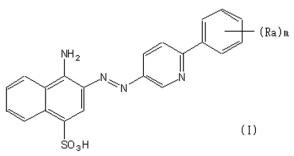
Novel Compounds for the Treatment of Glaucoma and Retinal Pigmentary Degeneration

VCP Inhibitors of Efficacy for Glaucoma and Retinal Pigmentary Degeneration

Professor Akira Kakizuka, Graduate School of Biostudies
Assistant Professor Hanako Ikeda, Graduate School of Medicine
Professor Nagahisa Yoshimura, Graduate School of Medicine



Some compounds, which develop as VCP inhibitors, showed strong neuroprotective effects for retinal neuronal cells, including ganglion cells and photoreceptor cells. They suffered in glaucoma and retinal pigmentary degenerations. Oral daily administration of these compounds to mouse models of retinal disorders, namely GLAST knockout mice as well as DBA/2J mice or rd10 mice, showed significant protection from cell death of ganglion cells or photoreceptor cells during treated periods, e.g. up to eight months for GLAST knockout mice. However, no apparent side effects were apparent.

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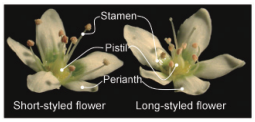
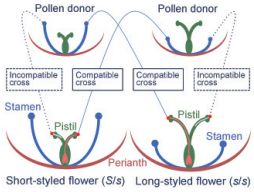
Nucleotide Sequences that Enable the Production Self-Fertilizing Buckwheat

Nucleotide Sequence Controlling Self-Incompatibility of Buckwheat

Assistant Professor Yasuo Yasui, Graduate School of Agriculture
Associate Professor Masashi Mori, Ishikawa Prefectural University





Buckwheat (Fagopyrum esculentum) is an annual crop produced in the world's temperate regions. Buckwheat flour is used in various ways to make noodles, bread, pancakes and other products. As it contains various nutrients, particularly proteins and minerals, it is known as a healthy food. However, buckwheat has a defective breeding trait, known as self-incompatibility. Thus, the yield of buckwheat is low compared with other major self-fertilizing crops. To make a high-yield buckwheat cultivar, it is necessary to break down the self-incompatibility system of buckwheat.

Assistant Prof. Yasui and Associate Prof. Mori have discovered a new gene, S-LOCUS EARLY FLOWEING 3 (S-ELF3), which plays an important role in the self-incompatibility system of buckwheat. The professors are now preparing to make a self-fertilizing buckwheat cultivar by breaking down the S-ELF3 gene using a transgenic or mutagenesis technique.

www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0031264

Gene Transfection using a Hydroxyapatite Microcapsule

Fabrication of a Hydroxyapatite Microcapsule for Gene Transfection

Professor Takeshi Yao, Graduate School of Energy Science
Assistant Professor Takeshi Yabutsuka, Graduate School of Energy Science

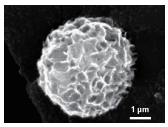


Fig.1 Hydroxyapatite (HA) microcapsule containing DNA in its inside

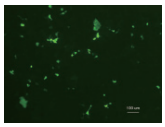


Fig.2 EGFP expression in fluorescent microscopy

Generally, genes are transfected using a vector virus, however, an alternative method is strongly desired because the use of a vector virus has risks of infection and canceration. Prof. Takeshi Yao and Assistant Prof. Takeshi Yabutsuka have fabricated a hydroxyapatite (HA) microcapsule containing DNA (as shown in Fig.1) for gene transfection. The hydroxyapatite microcapsule possesses high bioaffinity and is innocuous to the human body. They examined its effectiveness as follows. They fabricated the hydroxyapatite microcapsules containing EGFP, and then put them in the medium of human embryonic kidney 293 cells. After twenty-four hours, using fluorescent microscopy, they observed EGFP expression with higher efficiency than using a vector virus as shown in Fig.2. HA protects the genes from the acidic circumstance of matrix vesicles, and dissolves to let the genes out. The hydroxyapatite microcapsule is easy to fabricate in large quantities.

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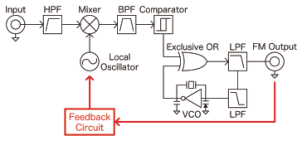
High Resolution Atomic Force Microscopy with Easy Operation

Method, Apparatus and Program to Widen the Detectable Range of Frequency Shift Detection for Vibrating Materials and Frequency Modulation Atomic Force Microscopy



Associate Professor Hirofumi Yamada, Graduate School of Engineering

Frequency-modulation atomic force microscopy (FM-AFM) is widely used as a high-resolution imaging and analysis tool in nanotechnology and nanoscience. In FM-AFM, the resonance frequency of a cantilever is modulated by the force between the tip and sample. To detect the frequency shift of the cantilever with a high sensitivity, a voltage-controlled oscillator (VCO) with a very narrow tuning range and a heterodyne circuit are used in the phase-locked loop (PLL). However, if the frequency shift exceeds the tuning range of the VCO, one has to adjust the local oscillator frequency in the heterodyne circuit.

A new PLL is equipped with a feedback circuit that automatically controls the local oscillator frequency. When the frequency shift of the cantilever exceeds the threshold frequency, the local oscillator frequency is shifted by a predetermined frequency so that the input frequency is always within the tracking range of the highly sensitive PLL.

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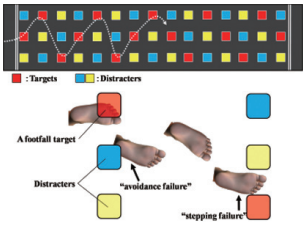
Applied Walking Program can Prevent Community-Dwelling Elderly from Falling



Assistant Professor Minoru Yamada, Graduate School of Medicine
Associate Professor Tomoki Aoyama, Graduate School of Medicine

Assistant Prof. Yamada and Associate Prof. Aoyama recently developed a new fall risk assessment, multi-target stepping (MTS) test to measure stepping accuracy in a simplified manner. In the MTS test, participants were instructed to consistently step on an assigned squares (footfall targets) for fifteen paces while avoiding other squares (distracters). Elderly subjects with a higher risk of falling showed a significantly higher rate of failure to avoid stepping on distracters (avoidance failure) compared to those with a lower risk of falling.

The current study was conducted to investigate whether a twenty-four-week exercise program in which elderly subjects performed the MTS task twice a week (MTS program) was effective in improving the subjects' ability to step precisely on footfall targets and, as a result, to prevent falling. The results showed that the MTS program is likely to improve stepping accuracy and physical performance, which could lead to a reduced risk of falling. Furthermore, the MTS program can prevent the risk of falling in community-dwelling elderly.

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