

INTRODUCTION

Biomaterials research in Japan

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Research into biomaterials in Japan began with dental materials, as in Western countries, and only conventional materials were studied in the early stages of research.

Since the early 1930s, various new types of organic polymers have been synthesized, mainly in Western countries, and their structure and properties have been investigated extensively. Their application began in industrial fields, but this was soon extended to the biomedical field. Leading scientists in Japan also began to be interested in biomedical applications of such polymers in the early 1970s. Their main interest was focused on the compatibility of these polymers with blood. Various surface modifications of polymers were attempted, and the effect of the structure and morphology of the surfaces of the polymers on their compatibility with blood was investigated. Some interesting papers were published from this research (Nakai *et al.* 1977; Suzuki *et al.* 1986; Ishihara *et al.* 1990; Okano *et al.* 1993), and other unique research paths have been developed; some of these are introduced in the present issue of this journal.

Prof. Iwata presents a novel observation on the dynamic behaviour of mesenchymal stem cells on nanogrooved patterns on polymers. Prof. Ishihara presents a novel surface modification of polymers based on the cell membrane structure, and its application in bionanodevices. Prof. Okano also presents a novel surface modification of polymers and its application to the recovery of contiguous living cell sheets for tissue engineering. Prof. Tabata presents novel examples of applications of polymers to cell scaffolds and drug delivery systems (DDSs) of biosignalling molecules for tissue engineering. Prof. Kataoka will present a novel control of the nanostructures of polymers and its application to DDSs for anti-cancer drugs and genes in the next issue of this journal.

High-purity alumina ceramics with high density were developed for electronic applications throughout the 1970s, and these were applied in artificial hip joints in

France in 1971. This was successful because alumina ceramics are superior in terms of their mechanical strength and chemical durability, as well as in their resistance to wear. Orthopaedic surgeons and dentists in Japan were very impressed with this trial, and initiated research into applications of alumina ceramics in orthopaedic surgery and dentistry. Medical-grade high-purity alumina ceramics were also produced in Japan, and widely used clinically (Oonishi *et al.* 2008).

In 1976, sintered hydroxyapatite was found to bond to living bone in both the USA and Japan. Allografts are not as popular in Japan as in Western countries, and, hence, synthetic bone substitutes are in demand. There has been extensive research in Japan into the synthesis and application of bone-bonding ceramics, the so-called bioactive ceramics. A unique bioactive ceramic called glass–ceramic A–W with a high mechanical strength and high bioactivity was developed and used clinically (Kokubo 2008; Yamamuro 2008). Various types of bioactive ceramics with different characteristics have been developed. Some of these are introduced in the present issue of this journal. Prof. Yoshikawa presents a novel preparation of porous hydroxyapatite and discusses its application to bone tissue engineering and clinical treatments in orthopaedic surgery. Prof. Ohtsuki presents novel bioactive materials that were designed based on their chemical reactivity in a body fluid.

The bone-bonding mechanism of bioactive ceramics has also been investigated extensively. Based on these results, a simulated body fluid (SBF) was proposed as a useful solution for evaluating the bone-bonding ability of a material *in vitro*, and has been registered as an ISO 23317 standard (Kokubo & Takadama 2006). It was assumed that, using this SBF, titanium metal could spontaneously bond to living bone through the apatite layer formed on its surface in the living body if it was subjected to NaOH and heat treatments to form sodium titanate on its surface. This assumption was shown to be correct using animal experiments. Thus, the prepared bioactive titanium metal was applied to an artificial hip joint and has been used clinically in Japan since 2007 (Kokubo *et al.* 2008).

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One contribution of 10 to a Theme Supplement ‘Japanese biomaterials’.

The advantage of using metals as a biomaterial is their high fracture toughness. However, they do have some disadvantages, such as the cytotoxicity of released ions and wear debris, high Young's modulus and poor biocompatibility. Metallic materials that showed a reduced influence of these disadvantages have been extensively investigated in Japan, as well as in Western countries. As a result, Ni-free stainless steel, shape-memory alloys, Co–Cr alloys and beta-type titanium alloys with low Young's modulus have been developed (Niinomi *et al.* 2005). Various surface modifications for improving the biocompatibility of metals have also been carried out. Prof. Hanawa introduces recent progress in the surface modification of titanium metal for improving hard-tissue compatibility and immobilization of biofunctional molecules on the metal surface in the present issue of this journal.

Recently, much attention has been paid to the unique properties of materials on the nanometre scale, and their applications in various fields. However, in such applications, their reactions with living cells, tissues and organs must be carefully assessed. Prof. Watari will present the effect of nanosized materials reacting with living organs in the following issue of this journal.

I hope this special issue of this journal will promote the international exchange of frontier biomaterials research, and contribute to further progress in the application and development of biomaterials.

REFERENCES

- Ishihara, K., Aragaki, R., Ueda, T., Watanabe, A. & Nakabayashi, N. 1990 Reduced thrombogenicity of polymers having phospholipid polar groups. *J. Biomed. Mater. Res.* **24**, 1069–1077. (doi:10.1002/jbm.820240809)
- Kokubo, T. 2008 Bioactive glass–ceramics. In *Bioceramics and their clinical applications* (ed. T. Kokubo), pp. 284–301. Cambridge UK: Woodhead Publishing.
- Kokubo, T. & Takadama, H. 2006 How useful is SBF in predicting *in vivo* bone bioactivity? *Biomaterials* **27**, 2907–2915. (doi:10.1016/j.biomaterials.2006.01.017)
- Kokubo, T., Takadama, H. T. & Matsushita, T. 2008 Titania-based materials. In *Bioceramics and their clinical applications* (ed. T. Kokubo), pp. 485–500. Cambridge, UK: Woodhead Publishing.
- Nakai, S., Nakaya, T. & Imoto, M. 1977 Polymeric phospholipid analog. 10. Synthesis and polymerization of 2-(methacryloyloxy)ethyl 2-aminoethyl hydrogen phosphate. *Macromol. Chem. Phys.* **178**, 2963–2967. (doi:10.1002/macp.1977.021781021)
- Niinomi, M., Hanawa, T. & Narushima, T. 2005 Japanese research and development on metallic biomedical, dental and healthcare materials. *JOM J. Miner. Metals Mater. Soc.* **57**, 18–24. (doi:10.1007/s11837-005-0076-3)
- Okano, T., Yamada, N., Sakai, H. & Sakurai, Y. 1993 A novel recovery system for cultured cells using plasma-treated polystyrene dishes grafted with poly(*N*-isopropylacrylamide)(MA). *J. Biomed. Mater. Res.* **27**, 1243–1251. (doi:10.1002/jbm.820271005)
- Oonishi, H., Kim, S. C., Oonishi Jr, H., Masuda, S., Kyomoto, M. & Ueno, M. 2008 Clinical applications of ceramic–polyethylene combinations in joint replacement. In *Bioceramics and their clinical applications* (ed. T. Kokubo), pp. 699–717. Cambridge UK: Woodhead Publishing.
- Suzuki, M., Kishida, A., Iwata, H. & Ikada, Y. 1986 Graft copolymerization of acrylamide onto a polyethylene surface pretreated with glow discharge. *Macromolecules* **19**, 1804–1808. (doi:10.1021/ma00161a005)
- Yamamuro, T. 2008 Clinical application of bioactive glass–ceramics. In *Bioceramics and their clinical applications* (ed. T. Kokubo), pp. 583–605. Cambridge UK: Woodhead Publishing.