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Leeds, 2 August 2011

**Japanese/European Collaborative 01 April 2010  
Pathological Society Grant Reference No: JC 2010 01**

Dear Sirs,

I would like to thank the Pathological Society of Great Britain and Ireland and the Japanese Society of Pathology for providing the funding to enable the development of a collaborative research project between Leeds and Tokyo/Yokohama.

Since the award was made, we have had three meetings (2 in Tokyo/Yokohama and one in Leeds) of the collaborative group consisting of Dr Tomio Arai, pathologist from the Tokyo Metropolitan Geriatric Hospital and co-applicant of this grant; Dr Yohei Miyagi and Dr Yoichi Kameda, both pathologists at the Kanagawa Cancer Centre in Yokohama; Dr Akira Tsuburaya and Dr Takaki Yoshikawa, both gastric cancer surgeons from the Kanagawa Cancer Centre. The meetings of the group were joined by my long standing collaborator Patrick Tan from Singapore and by Satoshi Morita, statistician from the Yokohama City University as well as trainee pathologists and surgeons.

During the first meeting in September 2010, the study protocol 'Predictive and prognostic factors in Japanese gastric cancer with and without adjuvant S1 chemotherapy' was discussed and amended and has subsequently obtained full ethical approval in Yokohama. Approximately

200 patients suitable for this retrospective study were identified by the Yokohama surgeons and all slides from the gastrectomy specimens were retrieved and ready for review when we met in September. We discussed and decided the sampling strategy at the first day of the meeting and then reviewed all slides from all cases and marked areas of interests for DNA extraction, RNA extraction, tissue microarray construction within 2 days by the four pathologists, a true slide marking marathon. As we were all sitting in the same room at the different microscopes, this provided us also with the opportunity to compare our diagnostic criteria and classifications.

As it is not possible to export paraffin blocks to the UK, the Yokohama pathology team were given the task to cut at a minimum 20 sections from each block which is equivalent to 60 sections per patient (tumour, normal and reserve) x 200 = 12,000 slides. All slides have been received in Leeds at the time of this report and the shipment costs of ~ £1500 were covered by the current grant.

Tissue microarrays have been constructed in duplicate by the Japanese collaborators lead by Dr Miyagi and the TMA blocks have also already been sent to Leeds. TMA blocks have been cut and first immunohistochemical stainings have been performed here in Leeds indicating that most but not all our Leeds protocols work on the Japanese material. As soon as all protocols have been adjusted, all TMAs will be stained in Leeds. The slides will then be scanned and scored jointly in the UK and in Japan via the internet.

After preliminary experiments to establish whether our DNA extraction protocol works equally well for the Japanese material, we are now extracting first of all the DNA from normal tissue which will be completed within the next 5 to 6 weeks. Part of this DNA will then be shipped to our collaborator to Singapore for SNP analysis of GSTP1, TYMS, DPD, TP, ERCC1 etc, markers known to be potentially related to response to therapy.

All marked HE stained slides of the Yokohama gastric cancer were also sent to Leeds as they were needed for the extraction process. These slides have all been scanned at 40x magnification using the Leeds Aperio Scanner facility. At the second meeting in Japan in April 2011, I trained the Japanese surgeons and pathologists how to access the images and perform morphometric analysis (first of all point counting to establish the tumour stroma ratio) using our Leeds web interface. The initial morphometric analysis will be performed by junior surgeons from Yokohama, whereas Tomio Arai and I will do the counterscoring and provide further training to the surgical research fellows if needed. I have received the first xml files for counterscoring a couple of weeks ago. The generation and analysis of the results from this morphometric analysis will still take a couple of months.

The data collection of the Japanese gastric cancer patient has been completed and this data set is currently being used together with my Leeds gastric cancer to compare the effects of TNM classification 6th ed versus 7th ed. between the two centres with two entirely different patient publications. A first draft of the manuscript has been circulated.

The next visit of some of the Japanese in Leeds is scheduled for 8<sup>th</sup>/9<sup>th</sup> September 2011 and the next meeting in Japan will be in February 2012 during the Japanese Gastric Cancer Association meeting where I and the Singapore collaborator have been invited as chairs and speakers.

We are all looking back to a very successful and enjoyable year of establishing this collaboration where many things have moved forward very quickly due to the hard work and commitment of all parties involved. The funding of the two Pathological Societies was used to cover slide shipment costs, scanning costs, reagents and part of the meeting costs and has been greatly appreciated by all involved. As soon as results from this work will be available, they will be presented at the meetings of both Pathological Societies.

Sincerely,



Dr Heike Grabsch, Leeds



Dr Tomio Arai, Tokyo