Contribution ID: **50** Type: **Poster**

# Precision medicine in radiotherapy; discover a potential biomarker for treatment resistance

Introduction
Radiotherapy is an important modality of therapy in cancer treatment. Despite of advances in technology and cancer genomics, treatment of cancer is still a big challenge, and the mutation signatures of radioresistant tumors have not yet been fully elucidated. Radiation therapy technique is evolving over time, as increasing of radiation conformity will increase therapeutic ratio, as well as the development of particle and heavy-ion therapy which provide hopes.

Precision cancer medicine is a treatment for cancer which uses the genetic information of individual tumors to guide the treatment, has become widespread in cancer treatment, especially in the field of clinical oncology. Advances in next-generation sequencing technologies provide the identification of genetic alterations that make tumor cells responsive to molecularly targeted drugs. This also showed the probability such genetic alterations may contribute to cancer cell radiosensitivity. However, genetic alterations profile in cancers associated with resistant to radiotherapy have not been fully elucidated.

Methods
We analyzed a unique set of clinical specimens from a uterine cervical cancer that repeatedly locally recurred after multiple rounds of radiotherapy. We performed next-generation sequencing with an Ion AmpliSeq Comprehensive Cancer Panel that covers 95.4% of the exons of the 409 cancer-related genes.

Results
Exon sequencing of 409 cancer-related genes in the treatment-naïve tumor and the tumors that recurred after initial and secondary radiotherapy identified (i) activating mutations in *PIK3CA* and *KRAS*, and putative inactivating mutations in *SMAD4*, as trunk mutation signatures that persisted over the clinical course; and (ii) mutations in *KMT2A* and *TET1* as acquired mutation signatures observed only in recurrent tumors after radiotherapy. Comprehensive mining of published in vitro genomics data pertaining to radiosensitivity revealed that simultaneous mutations in *KRAS* and *SMAD4*, which have not been described previously in uterine cervical cancer, are associated with cancer cell radioresistance.

Conclusion
The results of this study indicated that next-generation sequencing analysis of clinical specimens is a promising strategy to explore the mutation signatures that contribute to tumor radioresistance, which is worth pursuing with larger cohorts in the future.

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**Session Classification:** Paper Session 4: Radiobiology