Genome Research Center for Hematopoietic Diseases

Director
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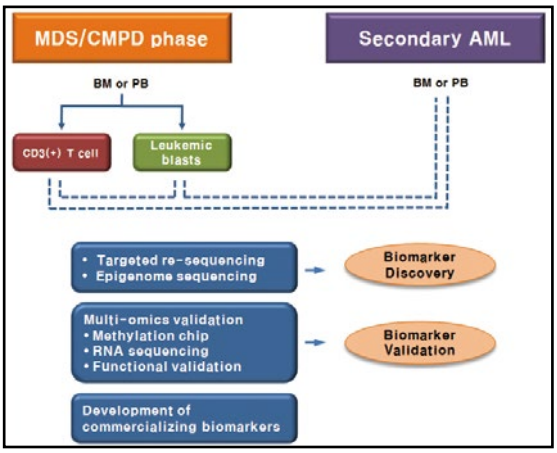
Major research goals

Despite targeted therapy, the drug resistance occurs in chronic myeloid neoplasm. We suggest the new mechanisms of resistance using the intratumorheterogeneicity. Further, we will discover novel mutations or biomarkers for prognosticators and druggable marker in targeted therapy-resistant chronic myeloid neoplasm. Eventually this study contributes to development of strategies that block the drug resistance.

Major research topics



1. Elucidation of tumorigenesis mechanism by using MDS/MPN-to-sAML progression model and epigenome sequencing platform based identification of cancer-specific regulatory mutational genes.
2. Unraveling clonal evolution of cytogenetic/genetic mutations in MDS/MPN cohorts treated with targeted therapy.
3. Discovery and validation of druggable target candidate to overcome therapeutic resistance by using multi-omics platforms.
4. DB building for epigenetic variations and development of early disease detection and kit by using Korean-specific genome signatures.

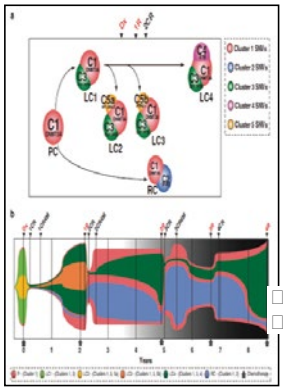
Major achievements

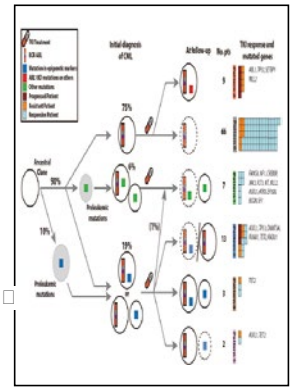
1. **Clonal dynamics over 9 years in an AML patient:** This study assesses clonal dynamics of a single AML patient over multiple relapses. Noticeably, a group of mutations that show anti-correlation with leukemia state(i.e. remission clone)
2. **Dynamic patterns of somatic mutations in CML:** This study captures the dynamics of somatic mutation using longitudinal samples in CML.

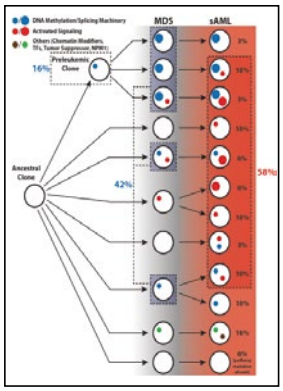
We found that mutation clearance in CML is not associated with successful TKI responses as well as the acquisition of mutation is a direct measure of treatment failure.

3. **Clonal origins of progression to secondary AML:** The purpose of this study is to profile the pattern of mutation acquisition in sAML patients using serial sequencing. From our study, we confirmed that sAML progression is correlated with allelic burden in genes associated with activated signaling pathway.

Representative figures of major achievements







❶. Clonal dynamics over 9 years in an AML patient.
❷. Dynamic patterns of somatic mutations in CML.
❸. Clonal origins of progression to secondary AML.

Major relevant publications

1. Kim TH, Yoshida K, Kim HJ, et al. Clonal dynamics in a single AML case tracked for 9 years reveals the complexity of leukemia progression. *Leukemia.* 2015;30(2):295-302
2. Kim TH, Tyndel MS, Kim HJ, et al. Spectrum of somatic mutation dynamics in chronic myeloid leukemiafollowing tyrosine kinase inhibitor therapy. *Blood.* 2016(Epub Ahead of Print)
3. Kim TH, Tyndel MS, Kim HJ, et al. The clonal origins of leukemic progression of myelodysplasia. *Blood.(*in revision)

Research networks

1. Zhaolei Zhang : Department of Computer Science, University of Toronto, Canada
2. Seishi Ogawa : Department of Pathology and Tumour Biology, Kyoto University, Japan
3. Dennis(Dong Hwan) Kim : Department of Medical Oncology, Princess Margaret Cancer Center, University Health Network, Faculty of Medicine, University of Toronto, Canada