WHITEPAPER

Meet the Marker: STAG1

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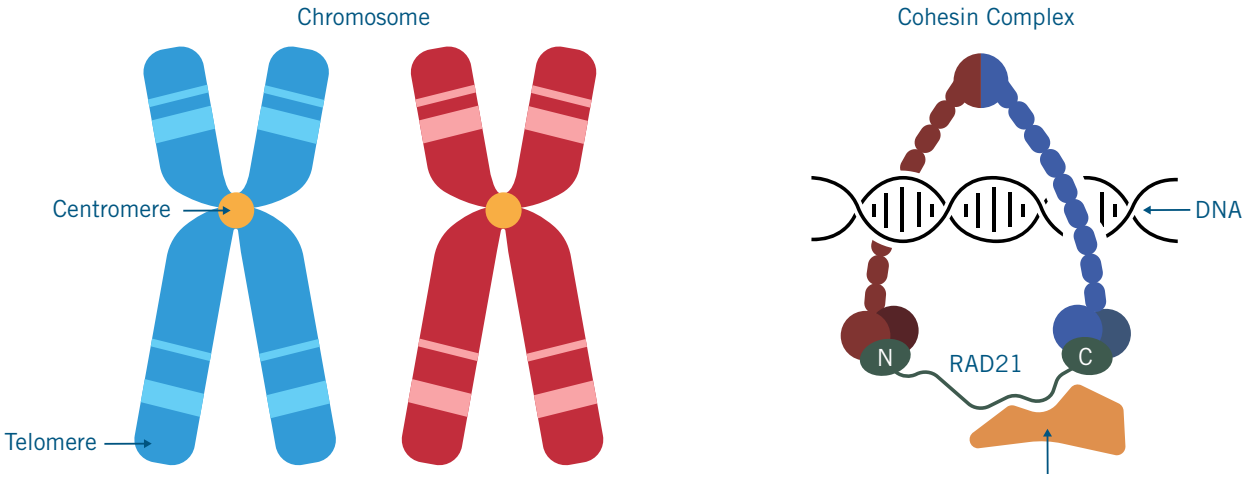
STAG1 (Stromal Antigen 1) is a component of cohesin, a ring-shaped protein complex whose purpose is to keep cellular genetic material correctly tethered and organized during various cellular processes such as DNA synthesis, cell replication, and DNA transcription.[2] By extension, it also plays an important role in the maintenance of chromatin structure, gene expression, and DNA repair.

The structure of cohesin contains two paralog STAG subunits, STAG1 and STAG2, which are thought to regulate cohesion in different domains of the chromosome. While STAG1 is primarily thought to regulate telomeric cohesion, STAG2 is believed to be primarily involved in centromeric cohesion.[1] These two paralogs overlap in function to enable one paralog to reciprocally compensate for the other in the event that the other is lost.[3] They are considered to be mutually exclusive in cancer formation, meaning that they do not tend to mutate at the same time in the same sample.[5] In fact, STAG2 tends to mutate at a far higher rate than STAG1 and is the most associated with cancer development.[1] STAG2 mutations have been detected in bladder cancer, Ewing sarcoma and acute myeloid leukemia.[4]

However, this mutually exclusive condition of STAG1 and STAG2 gives STAG1 significant immunotherapeutic potential. Studies have found that partial suppression of STAG1 triggers strong and selective anti-proliferative effects in cases of STAG2-mutant cancer models.[4] Furthermore, it appears that artificially induced genetic degradation of STAG1 results in the rapid cell death of STAG2-deficient cancer cells while leaving STAG2-wild type normal cells untouched.[4] This is referred to as "synthetic lethality," meaning that while one mutation may still allow the mutated cell to continue living and proliferating, functional or not, co-occurrence with other genetic mutations results in cell death.

In other words, STAG1 appears to show great promise in its potential to be a reliable and highly selective target for immunotherapy treatment of STAG2-mutant cancers due to the fact that a cell can only support the loss of either STAG1 or STAG2 and not both at the same time. Therefore, knocking out STAG1 will kill off any cells that already had a mutated copy of STAG2 while allowing normal, unmutated cells to survive.

Chromosome and Cohesin Complex



Given this promising outlook for the application of STAG1, Biocare is excited to offer a newly released STAG1 marker. To learn more about product offerings for STAG1, visit us at biocare.net or call 1-800-799-9499.

1. Arruda NL, Carico ZM, Justice M, Liu YF, Zhou J, Stefan HC, Dowen JM. Distinct and overlapping roles of STAG1 and STAG2 in cohesin localization and gene expression in embryonic stem cells. Epigenetics Chromatin. 2020 Aug 10;13(1):32. doi: 10.1186/s13072-020-00353-9.
2. Hill VK, Kim JS, Waldman T. Cohesin mutations in human cancer. Biochimica Et Biophysica Acta (BBA) - Reviews on Cancer, 1866(1), 1–11. https://doi.org/10.1016/j.bbcan.2016.05.002
3. Romero-Pérez L, Surdez D, Brunet E, Delattre O, Grünewald TGP. STAG Mutations in Cancer. Trends Cancer. 2019 Aug;5(8):506-520. doi: 10.1016/j.trecan.2019.07.001. Epub 2019 Jul 31. PMID: 31421907.
4. Van der Lelij, P., Newman, J. A., Lieb, S., Jude, J., Katis, V., Hoffmann, T., Hinterndorfer, M., Bader, G., Kraut, N., Pearson, M. A., Peters, J.-M., Zuber, J., Gileadi, O., & Petronczki, M. (2020). STAG1 vulnerabilities for exploiting cohesin synthetic lethality in stag2-deficient cancers. Life Science Alliance, 3(7). https://doi.org/10.26508/lsa.202000725
5. Yulan Deng, Shangyi Luo, Chunyu Deng, Tao Luo, Wenkang Yin, Hongyi Zhang, Yong Zhang, Xinxin Zhang, Yujia Lan, Yanyan Ping, Yun Xiao, Xia Li, Identifying mutual exclusivity across cancer genomes: computational approaches to discover genetic interaction and reveal tumor vulnerability, Briefings in Bioinformatics, Volume 20, Issue 1, January 2019, Pages 254–266 https://doi.org/10.1093/bib/bbx109