# Human Acrocentric Chromosome and their Association with Nucleolar Organizer Regions in Down Syndrome

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## Abstract

In human five chromosomal loci encode ~ 360 copies ribosomal genes are called nucleolar organizer regions (NORs). These are located on the short arm of the acrocentric chromo-somes. The exact role of NORs is not known but it helps in the assembly of ribosomes during cell-division (mitosis). In the present case study the Down syndrome case used as model of non – disjunction event because of having an extra copy of acrocentric chromosome become imperative to know the associations between acrocentric chromosomes and NORs sites asso-ciated transcriptional event. In this case high incidence of NORs expression (>60% / cell) were observed. However, this study of NORs explores the mechanism of transcription dur-ing neuronal differentiation causes “mental retardation” has not been documented earlier in the literature.

**Key words:** Acrocentric Chromosome, Nucleolar Organizer Regions, Down Syndrome
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## Introduction

Human ribosomal gene repeats are distributed among five nucleolar organizer regions located on the short arms of acrocentric chromosome i.e. 13 , 14,15, 21 and 22 [1]. These five chromosomal loci that encode the 360 copies of ribosomal gene are termed nucleolar organizer regions (NORs). NORs can be identified as secondary constric-tions on metaphase chromosomes and can be visualized by silver staining, due to the abundance of argyrophilic proteins [2]. Large multiple small nucleoli form around individual active NORs appear to fuse into one or a few large nucleoli as the cell grows during development through the cycle, a phenomenon commonly referred to as nucleolar fusion [3]. Eukaryotic nucleus is functionally divided into various chambers in nucleolus, where multi-ple loci from different chromosomes add to the formation of a functional nuclear compartment. [4,5].

These stages of ribosome synthesis are observed at the structural level [6,7] As the cell- cycle progress nucleoli form active NORs after exit from mitosis and these mini-nucleoli fuse to form large nucleoli incorporating multiple NORs. Nucleoli are the sites of rDNA transcription, rRNA processing and the assembly of ribosomes because nucleolus can participate in many other aspects of gene expression [8,9,10]

The uniqueness of the proteins (C23 and B24) for this distinct chromatin structure is uncertain, but likely to be responsible for transcription machinery and nucleolar ref-ormation [11]. Because of variation in the frequency of expression of NORs during cell-division has not been documented in literature with different clinical lesson hence the present case study becomes imperative to evaluate the frequency of NORs in Down syndrome pa-tient reported first time.

## Case Report

Proband female aged 17th months old suspected Down Syndrome Patient referred to Human Cytogenetics Labo-ratory, Centre of Experimental Medicine and Surgery, IMS-BHU for confirmation of diagnosis by chromosomal (karyotyping) chromosomal analysis were carried out us-ing lymphocytes cultures with RPMI-1640 . Cells were harvested after addition of colchicines to arrest mitosis and slides were prepared as routine procedure of labora-tory with Giemsa staining. Nucleolar organizer regions (NORs) are visualized using AgNOR procedure of Good pasture et al (1974). Figure-1 showing a representative karyotype having an extra copy of chromosome -21, conforming the Down syndrome patient. The distribution of satellite region and frequency of NORs expression were noticed in well spread metaphase plates as recognized in figure-2. The. frequency of NORs expression was evaluated within the D and G group chromosomes as marked by arrow head in figure-2. Interestingly, 60% of acrocentric chromosomes per metaphase cell shows +ve AgNORs expression

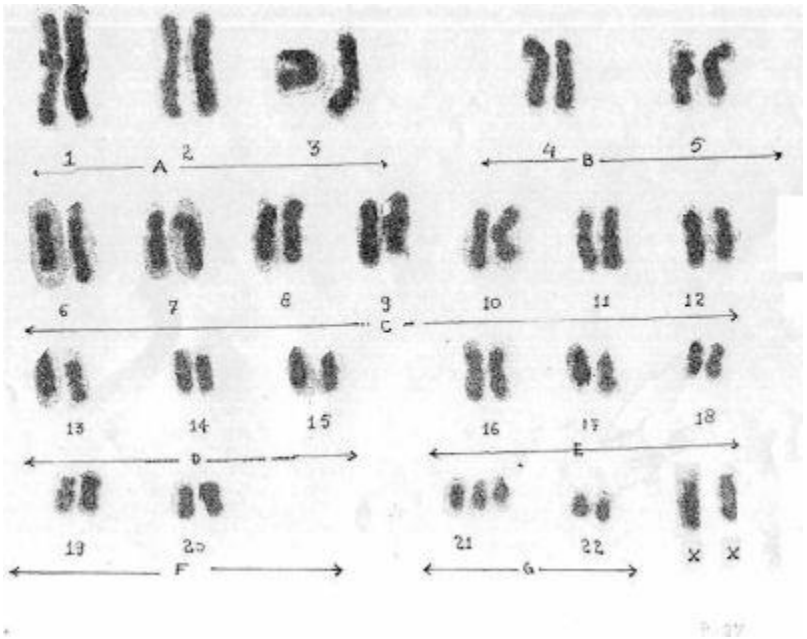


Fig. 1

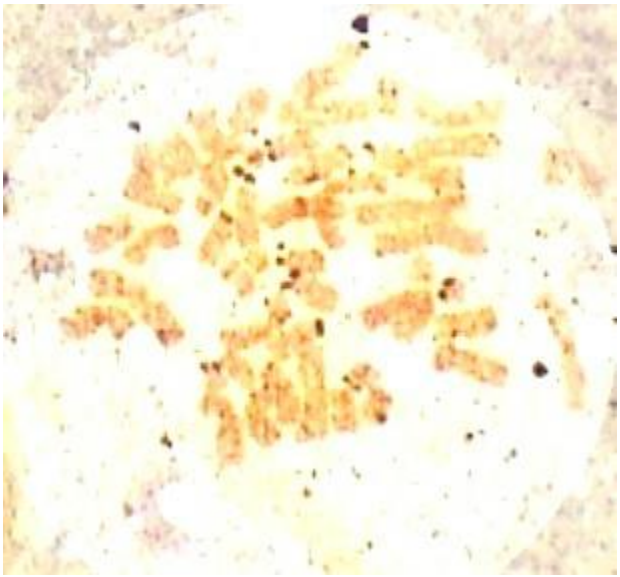

Fig. 2

Figures 1and 2. Representative karyotype showing an extra copy of chromosome no. 21 confirming the case of Down syndrome in (figure 1) while the metaphase showing + ve Ag NOR staining (figure 2) of the same case.

## Discussion

The present case study of NORs expression becomes im-perative to know the role of NORs during abnormal physiological condition while cells- division take place lead to non- disjunction events resulting unequal half of the cells carrying extra copy of chromosome 21. These regions directly associated with transcription machinery in this cell-cycle event [11]. NORs are located on short arm of acrocentric chromosomes having ribosomal gene, a cluster of an average 3 mega base pair in length (80 cop-ies of 43 kb repeats) [12]. Linkage studies reveals that NORs strictly does not follow the Mendelian pattern of inheritance, but it follows either Law of segregation or Independent assortment depending upon the nature of mating i.e. between Homozygote and Heterozygote and Heterozygote and Heterozygote. It is gernally believe that nucleolar in corporation of individual NOR is dependent on ribosomal gene transcription.

The present study showing high expression of active NORs in metaphase chromosomes may be because of nucleolar fusion in mental retarded patients. A conse-quence of this process is that multiple NORs can be found within a single nucleolus [13]. It is generally implicated that nucleolar incorporation of individual NORs is de-pendent on ribosomal gene transcription. It is tempting to speculate that heterochromatin sequences both proximal and distal end to the NORs of the short arm of acrocentric chromosome are responsible for either over or under ex-pression of C23 and B24proteins. This transcription ma-chinery is responsible for either non disjunction events or associated with neuronal proliferations which lead to such clinical lesson. However, the underline mechanism in this major dynamic nuclear reorganization involving addi-tional copy of chromosomes number 21 might have re-sponsible for over expression (NORs) during develop-ment and differentiation of central nervous system con-cerning gene protein interaction as model of Down Syn-drome has not been documented in the literature with clinical lesson. Although, further study are required to correlate major dynamic nuclear reorganization regions of acrocentric chromosome territories.

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