

## M3/M3v acute non lymphocytic leukemia (M3-ANLL)

## M3/M3v acute myeloid leukemia (AML M3/M3v)

## Acute promyelocytic leukemia (APL)

### Identity

#### Note

#### FAB criteria AML M3 :

great majority of cells are abnormal promyelocytes, with a characteristic pattern of heavy granulation  
characteristic cells contain bundles of Auer rods ("faggots")

#### FAB criteria AML M3v

minimal granulation, relative scarcity of cells with heavy granulation and cells containing multiple Auer rods. The nucleus of every cell in the peripheral blood is bilobed, multilobed or reniform, but the majority of cells are either devoid of granules or contain only a few fine azurophil granules. However, at least a few cells with all the cytoplasmic features of typical AML M3 are present. If these are overlooked, the cases are likely misdiagnosed as atypical monocytic leukemia. The atypical morphology is mainly a feature of the peripheral blood cells bone marrow morphology is closer to that of typical AML M3.

both subtypes show a very strong myeloperoxidase reaction and a negative reaction for non-specific esterase

#### Immunophenotype :

characteristic but not diagnostic myeloid phenotype  
CD33 positive, HLA-DR is generally absent  
in M3 but not M3v: characteristic light scatter pattern, strong unspecific fluorescence signal

#### WHO classification

distinct entity in category AML with recurrent genetic abnormalities:  
Acute promyelocytic leukemia ([AML](#) with [t\(15;17\)\(q22;q12\)](#) ([PML/RARA](#)) and variants)

### Clinics and Pathology

Epidemiology rare: 5 - 8 % of ANLL, incidence higher in Spain, Italy and Latinos;  
occurs at any age. predominantly adults in mid-life accounting for

	aprox. 5% of treatment related leukemias (t-AML)
Clinics	Low WBC in AML M3, high WBC in AML M3v; frequently associated with disseminated intravascular coagulation (DIC) and hyperfibrinolysis
Cytology	The cytomorphology of APL blasts is obviously different in the two subtypes: in AML M3, the abnormal promyelocytes show a heavy granulation and bundles of Auer rods; in AML M3v blasts have a non- or hypogranular cytoplasm or contain fine dustlike cytoplasmic granules that may not be apparent by light microscopy. Furthermore, M3v blasts show a typical bilobed nuclear configuration. This latter morphologic phenotype, together with missing granulation, often resulted in the misleading diagnosis of acute monocytic or myelomonocytic leukemia before the cytogenetic correlation of both AML M3 and M3v with t(15;17)(q22;q12) was observed. AML M3v accounts for approximately 1/3 of APL cases
Prognosis	Favourable if treated with an ATRA (all trans-retinoic acid) and anthracycline containing regimen: CR in >80% of cases, med survival: in most studies with ATRA treatment not reached yet, adverse prognosis factors: high WBC, <a href="#">FLT3</a> - internal tandem duplication (ITD), bleeding episodes.

## Cytogenetics

Cytogenetics	t(15;17)(q22;q12) leading to a PML-RARA-rearrangement on the
Morphological	molecular level variant translocations involving one or more chromosomes in addition to 15 and 17 are found in 2-5% of cases with PML-RARA-rearrangement cytogenetically cryptic PML-RARA-rearrangements are observed in 2-3% of APL cases
Additional anomalies	are observed in 35-45% of cases, most frequent: <a href="#">+8</a> , <a href="#">del(9q)</a> , <a href="#">ider(17)(q10)t(15;17)</a>
Variants	3 variant translocation involving RARA: <a href="#">t(11;17)(q23;q12)</a> leading to a fusion of RARA and <a href="#">PLZF</a> ; <a href="#">t(5;17)(q23;q12)</a> leading to a fusion of RARA and <a href="#">NPM</a> ; <a href="#">t(11;17)(q13;q12)</a> leading to a fusion of RARA and <a href="#">NuMA</a> . The cases with variant translocation have initially been reported as having APL morphology. However, morphological differences exist. Clinically important is that APL variant with t(5;17)(q12;q12) seems to respond to ATRA, while APL variant with t(11;17)(q23;q12) does not.

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