

Cytological composition of bone marrow in Athymic Nude RH-FoxN1^{nu} rats



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Introduction

Long-term pharmacology and safety evaluation of innovative human-derived cell therapy products require the use of immunocompromised animals to avoid immune-mediated destruction of injected human-derived cells. Athymic Nude rats represent an interesting alternative to broadly used Nude mice, particularly when implantation surgery is required, and animals of larger size are preferred.

In preclinical safety, bone marrow smears microscopic examination is an essential part of assessment of the hematopoietic system. Cytological evaluation of bone marrow smears is usually triggered by the detection of specific abnormalities at hematology, and/or blood smear microscopy and/or histology.

To date, there is no available published data regarding the cellular composition of bone marrow in RH-FoxN1^{nu} rats.

Objectives

The purpose of this study was to evaluate the cytological composition of the bone marrow of athymic RH-FoxN1^{nu} nude rats and to compare it with published data from non-athymic rats.

Materials and Methods

A total of 28 clinically healthy RH-FoxN1^{nu} rats (11 males, 17 females) provided by Envigo RMS, Netherlands, aged 9.5 months, were included in this study. Bone marrow smears were prepared after anesthesia and euthanasia following longitudinal incision of the proximal femoral bone. Two bone marrow smears were prepared on each animal and stained with May-Grünwald Giemsa.

Microscopic examination of bone marrow smears was performed by a Board-certified clinical pathologist. Complete differential cell count (approximately 300 cells) and morphological assessment at high power magnification were performed. Myeloid to erythroid ratios and the percentage of each individual cell types were calculated.

Results

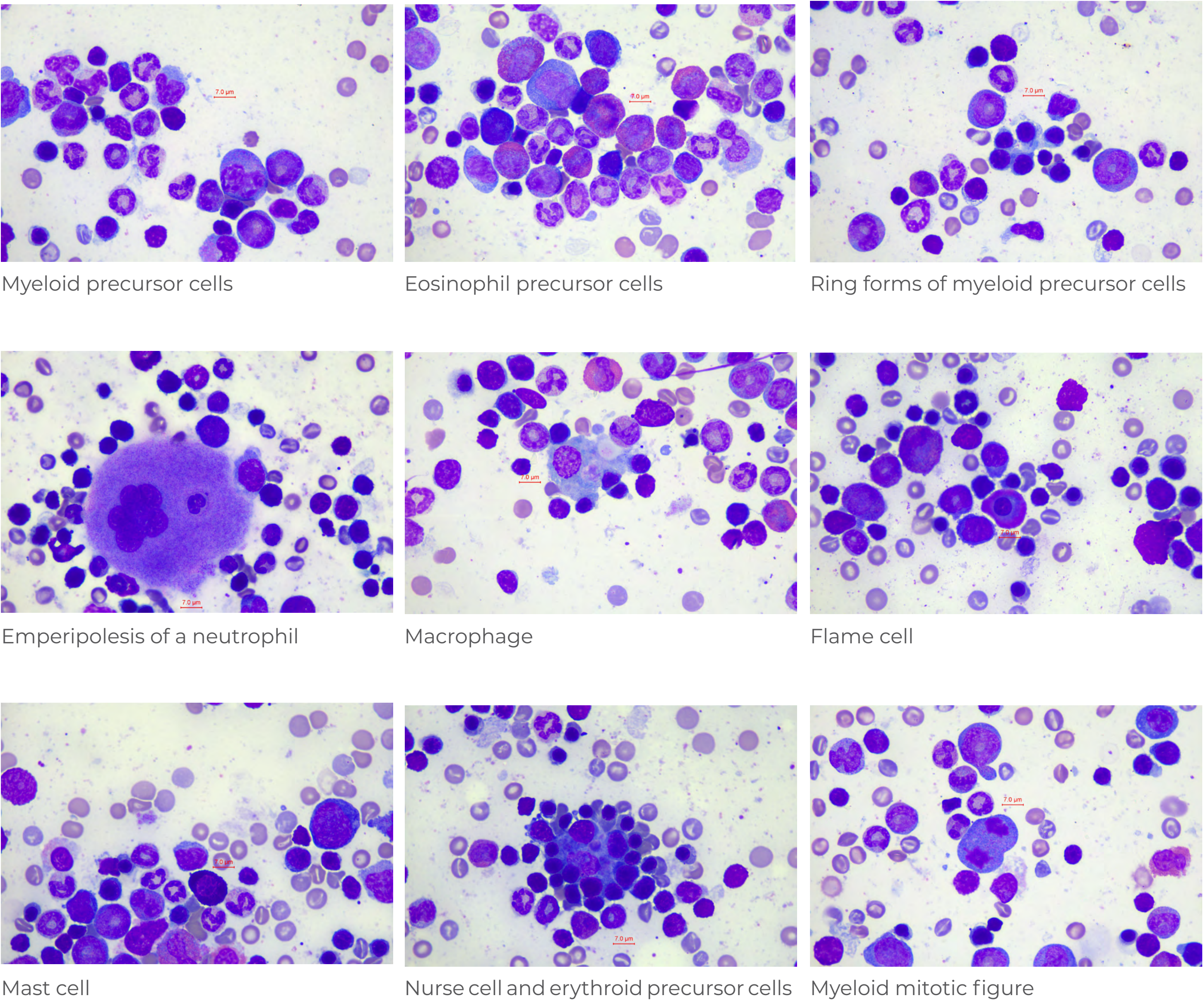
The mean percentages of each cell type are presented in Table 1.

Myeloid to erythroid ratios ranged from 0.66 to 3.16 (mean: 1.62). The erythroid cell line displayed rarely binucleated late precursors and nurse cells were rarely seen. Cells from granulocytic series showed similar morphological characteristics as Sprague-Dawley or Wistar Han rats with the presence of ring or doughnut forms. The lymphoid population was characterized by the presence of mature lymphocytes. Rare plasma cells and very rare flame cells were observed.

Emperipolesis of neutrophils on megakaryocytes was frequently observed. Non hematopoietic cellular components (osteoblasts,...) were observed in low numbers.

Table 1.
Bone marrow cytological composition from male and female RH-FoxN1^{nu} rats

Granulocytic series	Mean Percentage	SD
Myeloblasts	0.89	0.88
Promyelocytes	1.32	0.82
Neutrophilic myelocytes	2.24	1.06
Neutrophilic metamyelocytes	4.20	2.17
Band neutrophils	11.51	3.27
Segmented neutrophils	25.06	5.10
Eosinophils all stages	6.27	3.54
Basophils	0.35	0.38
Myeloid mitotic figures	0.71	0.64
Erythroid series		
Rubriblasts	0.46	0.31
Prorubricytes	0.64	0.38
Basophilic rubricytes	1.42	1.00
Polychromatophilic rubricytes	11.30	4.28
Metarubricytes	21.26	5.46
Erythroid mitotic figures	0.72	2.34
Lymphocytes		
Lymphocytes	11.96	3.61
Others		
Monocytes	0.48	0.31
Plasma cells	0.40	0.27
Mast cells	0.44	0.32
% Total granulocytic cells	52.56	10.55
% Total erythroid cells	35.80	9.24



CONCLUSION

The characterization of the cytological composition of the bone marrow is important to aid in accurate identification of hematopoietic precursor cells.

When compared with other rat strains commonly used in toxicological studies, we observed an increase in the proportion of eosinophils (all stages), an increase in emperipolesis of neutrophils on megakaryocytes and a decrease in the proportion of lymphocytes.

These results provide preliminary data of cytological bone marrow findings in athymic nude RH-FoxN1^{nu} rats.

References

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