Mechanisms of Ageing and Development xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Mechanisms of Ageing and Development

journal homepage: www.elsevier.com/locate/mechagedev

Role of human oocyte-enriched factors in somatic cell reprograming

Zaynab El-Gammal, Abdelrahman AlOkda, Nagwa El-Badri*

Center of Excellence for Stem Cells and Regenerative Medicine, Zewail City of Science and Technology, Egypt

ARTICLE INFO

Keywords:
Reprograming
Oocyte factors
Metabolic switch
Epigenetic transformation
Chromatin remodelling
Mitochondria

ABSTRACT

Cellular reprograming paves the way for creating functional patient-specific tissues to eliminate immune rejection responses by applying the same genetic profile. However, the epigenetic memory of a cell remains a challenge facing the current reprograming methods and does not allow transcription factors to bind properly. Because somatic cells can be reprogramed by transferring their nuclear contents into oocytes, introducing specific oocyte factors into differentiated cells is considered a promising approach for mimicking the reprograming process that occurs during fertilization. Mammalian metaphase II oocyte possesses a superior capacity to epigenetically reprogram somatic cell nuclei towards an embryonic stem cell-like state than the current factor-based reprograming approaches. This may be due to the presence of specific factors that are lacking in the current factor-based reprograming approaches. In this review, we focus on studies identifying human oocyte-enriched factors aiming to understand the molecular mechanisms mediating cellular reprograming. We describe the role of oocyte-enriched factors in metabolic switch, chromatin remodelling, and global epigenetic transformation. This is critical for improving the quality of resulting reprogramed cells, which is crucial for therapeutic applications.

1. Introduction

Cellular reprogramming refers to the erasure and remodelling of epigenetic marks, such as DNA methylation, during mammalian development or in cell culture (Reik et al., 2001). Disease models can be created by reprogramming somatic cells to possess the characteristics of diseased cells from patients. Additionally, reprogrammed cells from a patient can be used to generate autologous tissue-specific cells for transplantation in the case of an injury or degenerative disease. Moreover, these reprogrammed cells are important for drug screening and safety assessments (Singh et al., 2015). Cellular reprogramming has been achieved by somatic cell nuclear transfer (SCNT), cell fusion, and the ectopic expression of defined factors, such as OCT-4, SOX-2, KLF4 and c-MYC (OSKM) (Jaenisch and Young, 2008; Pasque et al., 2010; Yamanaka and Blau, 2010).

However, the ectopic expression of defined factors uses viral vectors to integrate OSKM genes in the host genome, which may increase the risk of tumour formation (Yamanaka and Blau, 2010). Additionally, other reprogramming methods, such as the transient expression of reprogramming factors by adenovirus vectors, plasmids or the direct delivery of reprogramming proteins, are mostly inefficient (Okita et al., 2008). Furthermore, studies comparing the DNA methylomes of human induced pluripotent stem cells (iPSCs) with that of embryonic stem cells (ESCs) have revealed that many iPSC lines retain the differential methylation patterns of the cells from which they are derived (Kim et al., 2010; Kim et al., 2011). This phenomenon is referred to as 'epigenetic memory', which (Maherali et al., 2007) is a challenge facing reprogramming methods and does not allow transcription factors to bind properly (Kim et al., 2010). Epigenetic memory impairs the differentiation capacity of iPSCs (Kim et al., 2010; Kim et al., 2011), gradually resolves the transcriptional and epigenetic differences with ESCs with increased passaging (Polo et al., 2010), and drives immunogenicity gene expression (Zhao et al., 2011). Thus, epigenetic memory negatively impacts the clinical application of iPSCs.

Somatic cells can be reprogrammed by transferring their nuclear contents into oocytes (Jaenisch and Young, 2008; Yamanaka and Blau, 2010; Hochedlinger and Jaenisch, 2006; Gurdon and Melton, 2008; Wilmut et al., 1997). Introducing specific oocyte factors into differentiated cells is thus considered a promising approach for mimicking the reprogramming process that occurs during fertilization. Global epigenetic analysis has shown that the mammalian metaphase II oocyte possesses a superior capacity to epigenetically reprogram somatic cell nuclei towards an ESC-like state than the current factor-based reprogramming approaches (Kim et al., 2010; Kim et al., 2011; Bar-Nur et al., 2011; Wakayama et al., 2006). This superior capacity may be due to the presence of specific factors that are lacking in the current factor-based

* Corresponding author at: Center of Excellence for Stem cells and Regenerative Medicine (CESC), Zewail City of Science and Technology, Ahmed Zewail road, October gardens, 6th of October City, Giza, Egypt.
E-mail address: nelbadri@zewailcity.edu.eg (N. El-Badri).

https://doi.org/10.1016/j.mad.2018.05.009
Received 8 March 2018; Received in revised form 23 May 2018; Accepted 30 May 2018

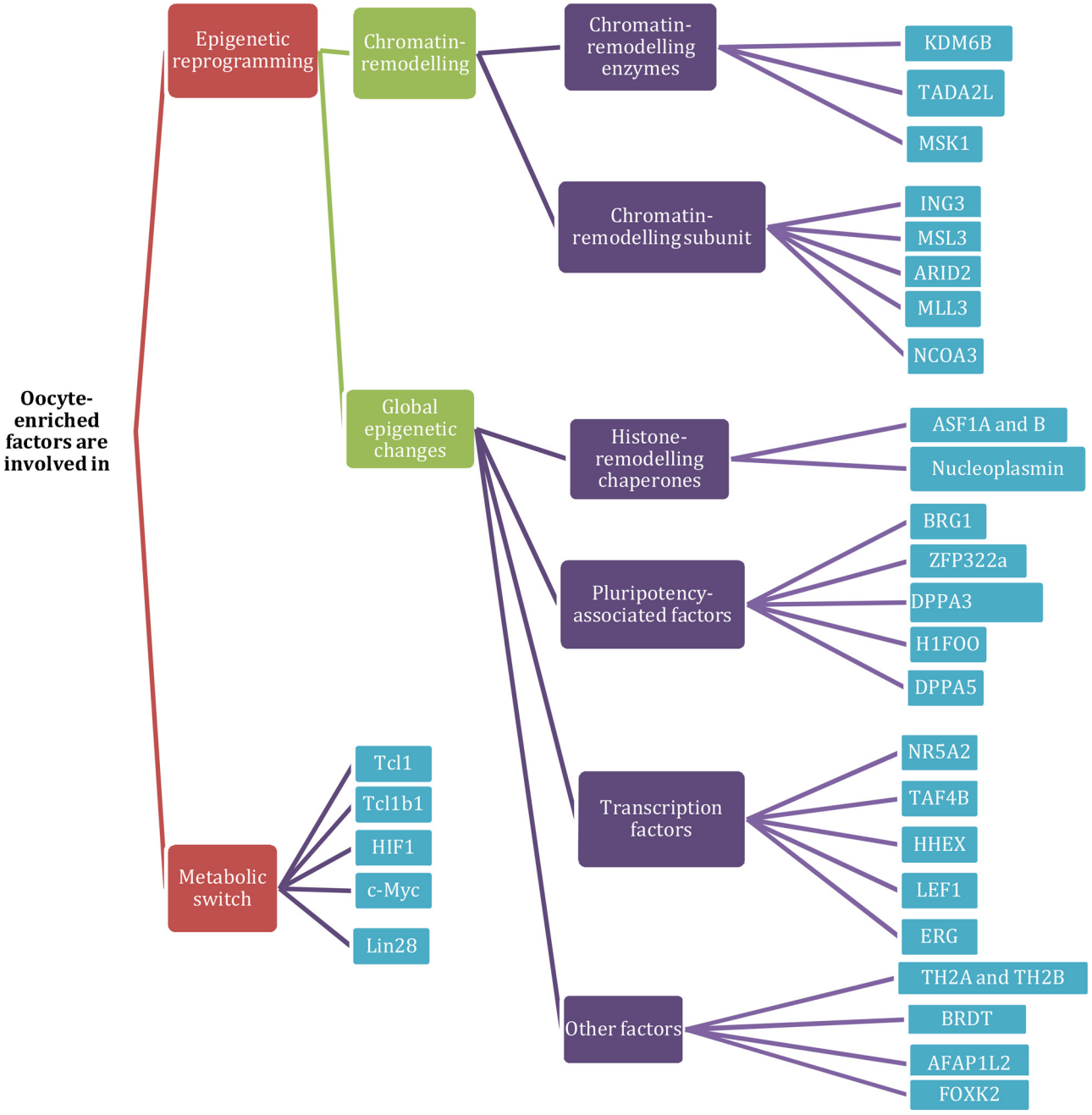

Fig. 1. Role of oocyte-enriched factors in inducing pluripotency.

reprogramming approaches. However, the yielded iPSCs vary widely in their developmental potential (Jaenisch and Young, 2008; Yamanaka and Blau, 2010; Kang et al., 2009; Zhao et al., 2009), as with the transcription factor-mediated reprogramming method. Thus, understanding the molecular mechanisms underlying somatic cell reprogramming by oocyte-enriched factors is critical for improving the quality of the resulting reprogrammed cells. Additionally, this information will broaden our understanding of fundamental topics regarding cell plasticity, identity and fate decisions (Vierbuchen and Wernig, 2012; Buganim and Jaenisch, 2012; Stadtfeld and Hochedlinger, 2010).

In this review, we focus on studies identifying human oocyte-enriched factors aiming to understand the molecular mechanisms mediating cellular reprogramming. We describe the molecular mechanisms of oocyte-enriched factors in metabolic switch, chromatin-remodelling, and global epigenetic transformation to achieve complete reprogramming (Fig. 1).

2. Oocyte-enriched factors and epigenetic memory

John Gurdon and Ian Wilmut suggested that oocyte-enriched factors are involved in loosening somatic chromatin, thereby providing the transcriptional regulatory apparatus access to repressed genes (Gurdon and Wilmut, 2011). Jason Awe and James Byrne suggested that these factors either remodel the chromatin architecture to a euchromatic state to be accessed by transcriptional regulators or promote a transformation in cellular fate towards an oocyte/totipotent or stem cell/pluripotent epigenetic state. This is referred to as the 'chromatin opening/fate transformative' (COFT) model (Awe and Byrne, 2013). They proposed two approaches for this model: the candidate oocyte reprogramming factors augmented approach and dynamic approaches. The augmented reprogramming model postulates that these factors will