UNIVERSITAS NEGERI MAKASSAR

BERLAYAR DAN BERTRANSFORMASI

60 Pemikiran untuk INDONESIA yang Berdaya Saing

DIPERSEMBAHKAN DALAM RANGKA
DIES NATALIS KE-60 UNM
TRANSFORMASI PENDIDIKAN BERKUALITAS BERBASIS ENTERPRENEURSHIP
DI ERA MERDEKA BELAJAR - KAMPUS MERDEKA

Badan Penerbit UNM

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Penyunting

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Kata Pengantar

Assalamu'alaikum Warahamatullahi Wabarakatuh

Puji Syukur Kehadirat Allah SWT atas limpahan rahmat dan hidayahNya sehingga dapat menyelesaikan buku yang dipersembahkan untuk Dies natalies ke-60 UNM. Salam dan Taslim tercurah kepada baginda Nabi Muhammad SAW, yang merupakan suri tauladan yang paling baik bagi ummat manusia hingga akhir zaman.

Selama 6 dasawarsa, Universitas Negeri Makassar telah memberikan kontribusi yang positif dan nyata bagi pembangunan sumber daya manusia di Indonesia pada umumnya dan di Kawasan Timur Indonesia pada khususnya. Selama 6 dasawarsa, dengan semangat pinisi sang legenda maritim menjadi bukti kegagahan para pelaut Nusantara, Universitas Negeri Makassar telah mengarungi berbagai samudera perubahan dan gelombang disrupsi zaman, memajukan pendidikan dan ilmu pengetahuan, untuk Indonesia yang berdaya saing.

"Berlayar" merupakan kata yang tepat untuk merefleksikan perjalanan Universitas Negeri Makassar dalam mengabdi mengembangkan ilmu pengetahuan dan teknologi. Dengan semangat pinisi berlayar nenek moyang pendahulu telah membuktikan bahwa mereka merupakan pelaut tangguh yang berhasil menaklukkan lautan dengan melintasi tujuh samudera. Pinisi merupakan satu-satunya kapal yang mampu berlayar mengarungi 5 benua. Demikian pula dengan Universitas Negeri Makassar yang telah selama 6 dasawarsa mengarungi "samudera" perubahan ilmu pengetahuan dan "benua" disrupsi zaman dan teknologi dengan tetap berkontribusi dalam pengembangan ilmu pengetahuan dan teknologi di tengah zaman yang berubah.

"Bertransformasi" merupakan kata yang tepat untuk merefleksikan perjalanan Universitas Negeri Makassar dalam beradaptasi dengan perubahan dan disrupsi zaman. Disrupsi yang ditandai dengan VUCA yang merupakan singkatan dari volatility, uncertainty, complexity, dan ambiguity memperhadapkan kita padaa perubahan yang sangat cepat, tidak terduga, dipengaruhi oleh banyak faktor yang sulit dikontrol, dan kebenaran serta realitas menjadi sangat subyektif, sehingga menuntut setiap organisasi mampu beradaptasi dan melakukan inovasi untuk menghadapi setiap disrupsi, khususnya berdaptasi dengan perubahan yang mampu mendukung implementasi merdeka belajar kampus merdeka.

Melalui hal tersebut, untuk memperingati 6 dasawarsa Universitas Negeri Makassar "berlayar" dan "bertransformasi" telah terkumpul 60 tulisan yang merupakan hasil riset atau pemikiran akademisi-akademisi Universitas Negeri Makassar yang pakar di bidangnya masing-masing untuk berkontribusi dalam meningkatkan kualitas sumber daya manusia dan pengembangan ilmu pengetahuan dan teknologi menuju Indonesia yang berdaya saing. 60 tulisan tersebut berdasarkan temanya masing-masing sesuai dengan filosofi dies natalis Universitas Negeri Makassar yang ke 60 tahun layak untuk diberikan judul: Universitas Negeri Makassar Berlayar dan Bertransformasi: 60 Pemikiran untuk Indonesia yang Berdaya Saing

Demikian perngantar ini, semoga kumpulan 60 tulisan ini dapat menjadi salah satu kontribusi UNM untuk Indonesia yang berdaya saing.

Wassalamu'alaikum Warahamatullahi Wabarakatuh

Rektor,

Prof. Dr. Ir. H. Husain Syam, M.TP., IPU., ASEAN Eng.

Cellular Function of Nuclear Pore Complex Proteins During Cell Mitosis

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Abstract
Nuclear pore complexes (NPCs), located on nuclear membranes of mammalian cells, are the main structure for molecular transport between cytoplasm and nucleus. These complexes are built by proteins called Nucleoporins (Nups), which vary depending on their molecular weight. Besides for transport, several Nups such as Rae1, Nup88, Nup358, Tpr, Nup62 and Nup58 have shown their roles in mitotic processes. In this article we review the structure of Nups, the process of cell mitosis, and how Nups involve in the process. Immunostaining examination showed that several nucleoporins such as Nup62 and Nup58 localize at the centrosome and mitotic spindle during mitosis. In addition, Nup58 is also found in midbodies. We conclude that Nups have important role in mitosis and cytokinesis.

Keywords: *Nuclear pore complexes (NPCs), Nucleoporins (Nups), nuclear membranes, mitotis, cell division*

I. Introduction

Nuclear envelope separates the nucleoplasm and cytoplasm in eukaryotic cells across which macromolecules are transported. DNA replication and transcription occur in the nucleoplasm whereas protein translation occur in the cytoplasm. Thus, the transport of proteins, RNA and ribonucleoprotein particles into and out of nucleus is required. This trafficking occur in the NPCs which are embedded in pores of the nuclear envelope (Antonin, Ellenberg, & Dultz, 2008). The NPC form large aqueous transport channels that mediate and control the bidirectional exchange of macromolecules between the nucleus and cytoplasm (Lin & Hoelz, 2019) (figure 1).

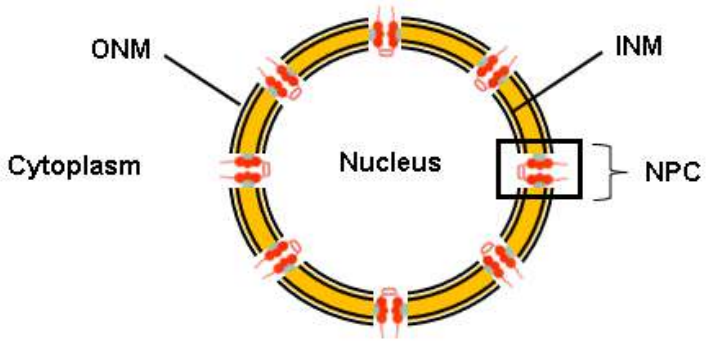

Figure 1. Schematic representation of nuclear pore complexes (NPC). NPC is anchored to nuclear envelope in eukaryotic cells by a membrane layer that surrounds the scaffold layer. This scaffold layer provides structure and serves as an anchor for nucleoporins (Nups). ONM=outer nuclear membrane; INM=inner nuclear membrane

NPCs are assembled as a central nano-turnstiles with filaments by a group of proteins called nucleoporins (Nups) which extend into the nucleus and cytoplasm (Sakuma & D'Angelo, 2017). In recent years, it has been revealed that Nups play various alternative roles unrelated to nuclear transport (Juhlen & Fahrenkrog, 2018; Wong & D'Angelo, 2016), including mitotic roles (Dawlaty et al., 2008; Linder et al., 2017). In this article we discuss the involvement of Nups in the cell division and the methods for its examination. To gain more understanding, we first review the structure of Nups, and the stages in cell mitosis.

II. Research Method

We use literature review by searching references using keywords such as “nucleoporin”, “Nup”, “Nuclear Pore Complex”, and “cell division”..

III. Findings and Discussions

1. The Structure of NPC

The molecular mass of NPC in mammals is around ~60–125 MDa (Stavru et al., 2006). Every Nup is present in copies of eight or multiples of eight due to the eightfold symmetry of pores hence each building blocks of the NPC is built by 500–1000 Nups which are biochemically connected with each other in stable subcomplexes (D'Angelo & Hetzer, 2008). The subcomplexes of Nups are Y-complexes, inner ring complex, transmembrane complex, Nup62 complex, cytoplasmic complex, and nuclear basket complex (Figure 2). Nups have a very limited set of domains, such as β-propellers, α-solenoids, phenylalanine-glycine (FG) repeats, coiled-coiled and transmembrane domains, all of which are soluble, except three transmembrane proteins that are believed to anchor the NPC to the NE (Stavru et al., 2006).

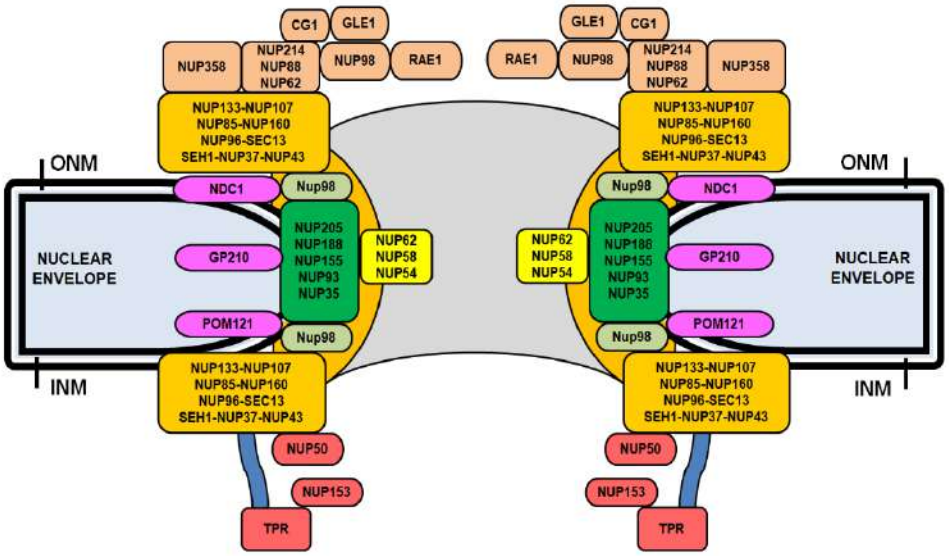

Figure 2. Structural organization of conserved NUPs from human. Orange :Y complexes; green: inner ring complex; purple: the transmembrane NUPs; yellow: NUP62 complex; brown: cytoplasmic complexes; red: nuclear basket complexes

During interphase, macromolecules trafficking between the cytoplasm and the nucleus in the cells rapidly occurs, controlled by NPCs (Lim & Wong, 2018; Wong & D'Angelo, 2016). The transport pathways are highly regulated by intracellular gradient of the GTPase Ran with a high concentration of RanGTP in the nucleoplasm and a high concentration of RanGDP in the cytoplasm which are maintained by the compartmentalised localisation of the Ran regulators RCC1, the Ran guanine nucleotide exchange factors (RanGEF) and the Ran GTPase activating protein (RanGAP1) (Chatel & Fahrenkrog,

2011). The process involves cargo proteins containing a nuclear localisation signal (NLS) or a nuclear export signal (NES) and transport receptors.

When mammalian cells enter mitosis, NPCs and nuclear lamina are disassembled during nuclear envelope breakdown (NEBD) (Dultz et al., 2008; Martino et al., 2017). Formerly, Nups were thought to remain latent in the cytoplasm during mitosis, awaiting NPC reassembly, but it has been unravelled that they play important roles in cell division, controlling gene expression, chromatin maintenance and mitotic progression (Juhlen & Fahrenkrog, 2018; Wong, 2015).

2. Mitosis Process

Based on the physical state of the chromosomes and spindle, mitosis involves five phases; prophase, prometaphase, metaphase, anaphase, and telophase (Paweletz, 2001). Cytokinesis, which is the final physical cell division that follows telophase, is sometimes considered a sixth phase of mitosis (Figure 3). Mitosis results in daughter cells with identical genetic compositions (O'Connor, 2008).

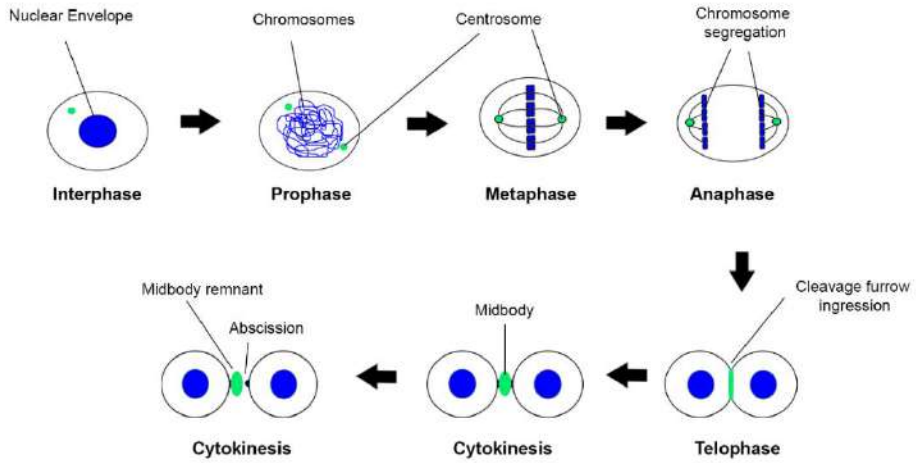

Figure 3. Schematic diagram illustrating cell stages from interphase to cytokinesis in animal cells

Mitosis begins with prophase, during which chromosomes continuously condensates until metaphase. The spindle begins to form as the two pairs of centrioles move to opposite poles and microtubules begin to polymerize from the duplicated centrosomes (Alberts, et al, 2002). Prometaphase begins with the abrupt breakdown of the nuclear membrane into many small vesicles that will eventually be divided between the future daughter cells. Microtubules rapidly assemble and disassemble as they grow out of the centrosomes, seeking out attachment sites at chromosome kinetochores, platelike structures located on one face of each sister chromatid

at its centromere. Finally, chromosomes are pulled and tugged in opposite directions by microtubules (O'Connor, 2008).

During metaphase centromeres of all chromosomes line up at the equator of the spindle, causing them easily visualized. At this stage cells can be experimentally arrested with mitotic poisons such as colchicine. A complex checkpoint mechanism determines whether the spindle is properly assembled, allowing the cells enter anaphase. Abrupt separation of sister chromatid marks the anaphase. This stage has two parts; movement of the chromosomes toward the spindle poles as the kinetochore microtubules shorten, and the move and separation of the spindle poles as the non-kinetochore microtubules move past each other, (Li et al., 2009; O'Connor, 2008; Gorbsky G. J., 2015).

Mitosis ends with telophase, at which the chromosomes reach the poles. The nuclear membrane reforms, whereas the chromosomes begin to decondense into their interphase conformations. Telophase is followed by the division of the cytoplasm into two daughter cells called cytokinesis (Cooper G. M., 2000; O'Connor, 2008)

3. Roles of Nups in Mitosis

Recently, several Nups have been reported to function at kinetochores, centrosomes and spindles during mitosis (Linder et al., 2017; Lussi et al., 2010). During metaphase Nups often remain in subcomplexes and are dispersed in the cytoplasm or associated with mitotic structures, such as the spindle or kinetochores. Nups reassemble to reform NPCs when the nuclear envelope is reformed at the end of anaphase (Chatel & Fahrenkrog, 2011). Using conventional confocal microscopy and live cell imaging techniques, it has been demonstrated that Nup Rae1(Funasaka et al., 2011; Wong, 2010), Nup88 (Hashizume, Nakano, Yoshida, & Wong, 2010), Tpr (Dewi et al., 2018; Kobayashi, Hashizume, Dowaki, & Wong, 2015; Nakano, Funasaka, Hashizume, & Wong, 2010), Nup358 (Hashizume, Kobayashi, & Wong, 2013), Nup62 (Hashizume, Moyori, et al., 2013; Hazawa et al., 2018) and Nup58 (Hartono et al., 2019) exert mitotic function (Nakano et al., 2011).

Nup62 plays a novel role in centrosome integrity during mitosis (Hashizume, Moyori, et al., 2013; Hazawa et al., 2018). Nup62 has been found to localize on the mitotic spindles and centrosomes during cell division (Hashizume, Moyori, et al., 2013). The centrosome has been shown to contribute in abscission and many centrosomal proteins have also been found to localize to the midbody ring. Indeed, Nup62 also transiently localizes to midbody ring at the end of abscission. Knockdown of Nup62 induced significantly higher numbers of multipolar spindles compared with controls (Hashizume, Moyori, et al., 2013)

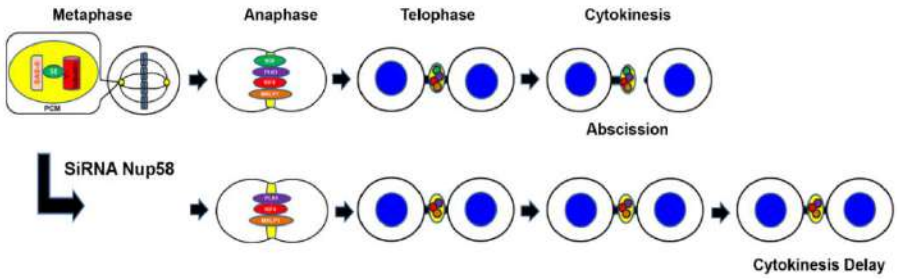

Figure 4. Speculative working model for Nup58 during mitotic progression and cytokinesis. Absence of Nup58 during cytokinesis caused delay from midbody maturation to final abscission. Green circle indicate Nup58

Using immunofluorescence assay, live cell imaging and STED nanoscopy, it has also been demonstrated that Nup58 transiently localizes to the centrosomes and the midbody—a bipolar microtubule array that assembles between separating sister chromatids (Johnson, Wright, & Ghashghaei, 2017)—during cytokinesis (Hartono et al., 2019) (Figure 4). Nup58 was detectable at mitotic spindle poles or centrosomal regions during prophase to anaphase and colocalized with some centrosome marker proteins such as γ-tubulin and SAS-6. Nup58 also gradually accumulated into spindle-like structures and colocalized with α-tubulin, a protein which plays critical roles during chromosome segregation. Nup58-depleted monopolar spindle cells induce mitotic catastrophe, aneuploidy, and eventually cell death. Thus, Nup58 play important roles in temporal regulation of telophase, cytokinesis, and abscission.

IV. Conclusion

Nucleoporins as the components of nuclear pore complex plays important roles not only in molecular trafficking between nucleoplasm and cytoplasm but also in temporal regulation of mitosis.

V. Acknowledgement

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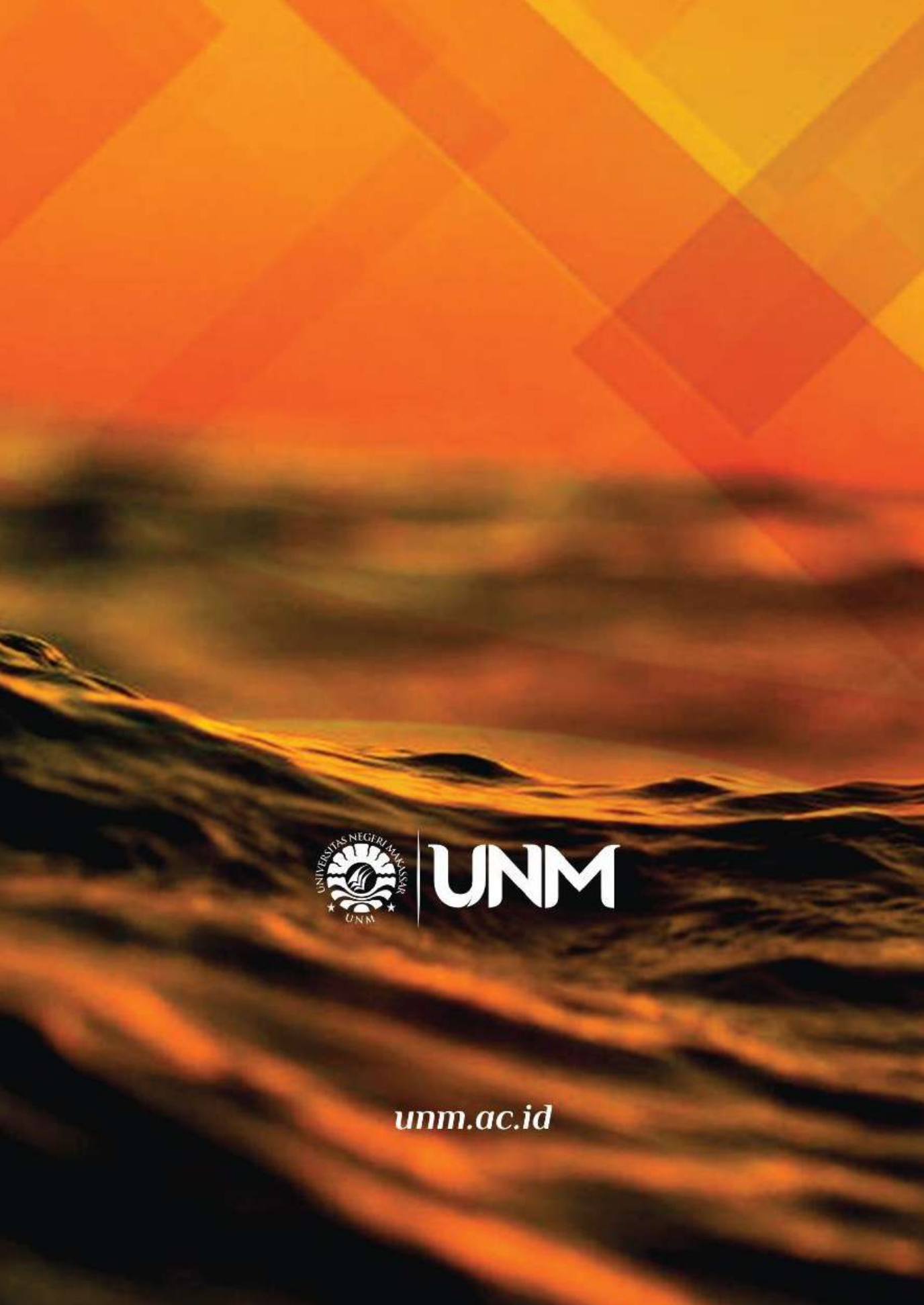
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