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SHORT *mre11Δ* TELOMERES IN *SACCHAROMYCES CEREVISIAE* DO NOT SHORTEN FURTHER UNDER THERMAL STRESS, IN CONTRAST TO LONG *pif1Δ* TELOMERES: POTENTIAL BIOMEDICAL IMPLICATIONS

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Telomeres are DNA-protein complexes capping chromosomal ends to secure genomic integrity in all eukaryotes. Many genes are involved in telomere maintenance. Mutations in those genes lead mostly to shortening and (less frequently) to lengthening of telomeres, which impairs their functionality. In humans, telomere attrition is linked to diseases. Beyond mutations, many stress factors contribute to alteration of telomere length (TL). Budding yeast, Saccharomyces cerevisiae, is a popular model for studying telomere biology. Thermal stress was one of the first among discovered extrinsic factors causing telomere shortening in budding yeast, a species with constitutive expression of telomerase. Temperature-induced decline in TL is known as Tmp- phenotype. This vivid phenomenon highlights possibilities to manipulate TL by exogenous factors. Here we show that mre11Δ mutants with very short telomeres do not generate Tmp- phenotype while pif1Δ mutants possessing very long telomeres do generate it and reduce their TL to the level in wild type cells grown under normal conditions. The absence of Tmp- phenotype itself could be a generic feature for phenotyping other mutants responding to heat in the same way. In addition, mre11Δ mutants exposed to elevated temperature manifested altered telomeric DNA patterns resembling those in type I survivors. These patterns are thought to result from recombinational processes within telomeric DNA. We discuss the relevance of our findings to fundamental and applied research.

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***Key words*:** *Saccharomyces cerevisiae, MRE11 deletion, PIF1 deletion, telomere attrition, thermal stress, MMS (methyl methanesulfonate), hydrogen peroxide.*

КОРОТКІ ТЕЛОМЕРИ *mre11Δ* У *SACCHAROMYCES CEREVISIA*Е НЕ СКОРОЧУЮТЬСЯ ЩЕ БІЛЬШЕ ПІД ВПЛИВОМ ТЕРМІЧНОГО СТРЕСУ НА ВІДМІНУ ВІД ДОВГИХ ТЕЛОМЕР *PIF1Δ*: ПОТЕНЦІЙНІ БІОМЕДИЧНІ НАСЛІДКИ

Теломери — це ДНК-білкові комплекси, що закривають кінці хромосом для забезпечення цілісності геному у всіх еукаріотів. Численні гени беруть участь у підтримці теломер. Мутації в цих генах здебільшого призводять до скорочення, а рідше — до подовження теломер, що порушує їхню функціональність. У людей скорочення теломер пов'язане із захворюваннями. Окрім мутацій, на зміну довжини теломер (TL) впливають численні фактори стресу. Пекарські дріжджі, *Saccharomyces cerevisiae*, є популярною моделлю для вивчення біології теломер. Термічний стрес був одним із перших виявлених зовнішніх факторів, що спричиняють скорочення теломер у пекарських дріжджах — виду з конститутивною експресією теломери. Спричинене температурою скорочення TL відоме як фенотип Tmp-. Це яскраве явище підкреслює можливості маніпулювання TL за допомогою екзогенних факторів. Тут ми показуємо, що мутанти *mre11Δ* з дуже короткими теломерами не генерують фенотип Tmp-, тоді як мутанти *pif1Δ*, що мають дуже довгі теломери, генерують його та скорочують свою TL до рівня клітин дикого типу, вирощених за нормальних умов. Сама відсутність фенотипу Tmp- може бути загальною ознакою для фенотипування інших мутантів, які реагують на тепло у такий же спосіб. Крім того, мутанти *mre11Δ*, піддані впливу підвищеної температури, демонстрували змінені структури теломерної ДНК, схожі на ті, що спостерігаються у вижилих типу I. Вважається, що ці структури є результатом процесів рекомбінації в теломерній ДНК. Ми обговорюємо значення наших результатів для фундаментальних та прикладних досліджень.

Ключові слова: *Saccharomyces cerevisiae*, делеція *MRE11*, делеція *PIF1*, скорочення теломер, термічний стрес, MMS (метилметансульфонат), пероксид водню.

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