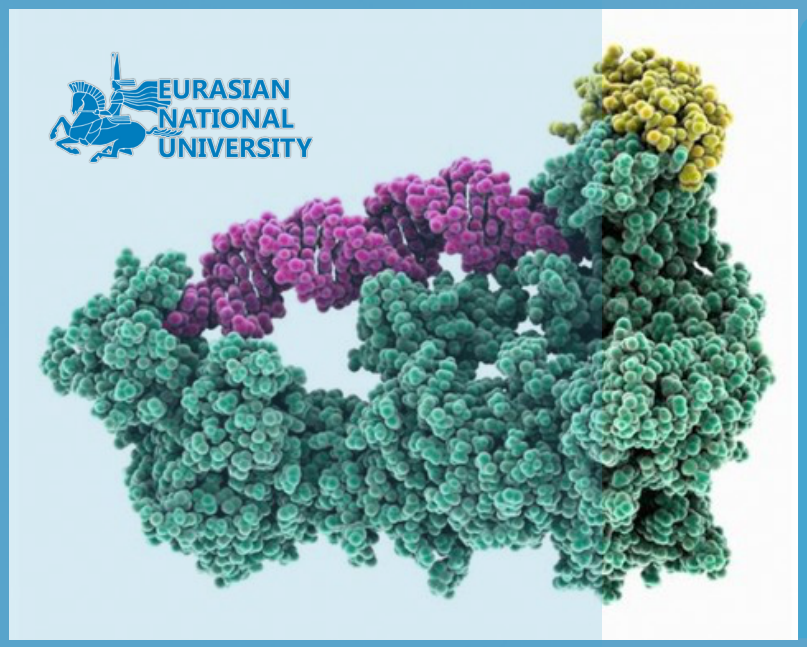
ҒЫЛЫМ ЖӘНЕ ЖОҒАРЫ БІЛІМ МИНИСТРЛІГІ
МИНИСТЕРСТВО НАУКИ И ВЫСШЕГО ОБРАЗОВАНИЯ



Л.Н. ГУМИЛЕВ АТЫНДАҒЫ
ЕУРАЗИЯ ҰЛТТЫҚ УНИВЕРСИТЕТІ

ЕВРАЗИЙСКИЙ НАЦИОНАЛЬНЫЙ
УНИВЕРСИТЕТ ИМЕНИ
Л.Н. ГУМИЛЕВА

"ОМАРОВ ОҚУЛАРЫ: XXI ҒАСЫРДЫҢ БИОЛОГИЯ ЖӘНЕ БИОТЕХНОЛОГИЯСЫ" АТТЫ ХАЛЫҚАРАЛЫҚ ҒЫЛЫМИ ФОРУМНЫҢ БАЯНДАМАЛАР ЖИНАҒЫ

СБОРНИК МАТЕРИАЛОВ МЕЖДУНАРОДНОГО НАУЧНОГО ФОРУМА "ОМАРОВСКИЕ ЧТЕНИЯ: БИОЛОГИЯ И БИОТЕХНОЛОГИЯ XXI ВЕКА"

АСТАНА, ҚАЗАҚСТАН
11 СӘУІР 2024 ЖЫЛ

АСТАНА, КАЗАХСТАН
11 АПРЕЛЯ 2024 ГОД

УДК 57 (063)
ББК 28.0
Ж 66

«Омаров оқулары: XXI ғасыр биология және биотехнологиясы» халықаралық ғылыми форумының баяндамалар жинағы. – Астана: Л.Н. Гумилев атындағы Еуразия ұлттық университеті, 2024. – 284 б., қазақша, орысша, ағылшынша.

Сборник материалов международного научного форума «Омаровские чтения: Биология и биотехнология XXI века». – Астана. Евразийский национальный университет имени Л.Н. Гумилева, 2024. – 284 с., казахский, русский, английский.

ISBN 978-601-337-977-7

Жинақ «Омаров оқулары: XXI ғасыр биология және биотехнологиясы» атты халықаралық ғылыми форумына қатысушылардың баяндамаларымен құрастырылған. Бұл басылымда биология, биотехнология, молекулалық биология және генетиканың маңызды мәселелері қарастырылған. Жинақ ғылыми қызметкерлерге, PhD докторанттарға, магистранттарға, сәйкес мамандықтағы студенттерге арналған.

Сборник составлен по материалам, представленным участниками международного научного форума «Омаровские чтения: Биология и биотехнология XXI века». Издание освещает актуальные вопросы биологии, биотехнологии, молекулярной биологии и генетики. Сборник рассчитан на научных работников, PhD докторантов, магистрантов, студентов соответствующих специальностей.

ISBN 978-601-337-977-7

УДК 57
ББК 28
О-58

Science and BioTechnology, 6(1-3), 145-156. [Retrieved from: https://doi.org/10.1007/s00253-010-2589-0]

УДК 57.579.64

MHETase enzyme

Zhakenov Daniyal Shokhanovich, Turpanova Rauza Masgutovna
L.N.Gumilyov Eurasian National University, Astana, Kazakhstan
zhakenov.daniyal@mail.ru

Plastic pollution represents a global environmental crisis. In response, microbes have evolved the ability to utilize synthetic polymers as carbon and energy sources. Recently, it was reported that Ideonella sakaiensis secretes a dual-enzyme system to degrade polyethylene terephthalate (PET) into its constituent monomers. Specifically, Ideonella sakaiensis PETase depolymerizes PET, releasing soluble products including mono(2-hydroxyethyl)terephthalate (MHET), which is cleaved by MHETase to terephthalic acid (TPA) and ethylene glycol (EG) [1].

Characterization of Ideonella sakaiensis revealed the enzyme PETase, which is a cutinase-like serine hydrolase that attacks the PET polymer, releasing bis-(hydroxyethyl)terephthalate (BHET), mono(2-hydroxyethyl)terephthalate (MHET) and TPA. PETase cleaves BHET to MHET and EG, and the soluble product of MHET is further hydrolyzed by MHETase to form TPA and EG. The structure and function of the MHETase enzyme is much less understood: to date there are few published studies on the structure and development of MHETase. To this end, this article combines information on the structure and function of MHETase and the results of bioinformatics analysis.

Functional annotation

MHETase was originally assigned to the Tannase family of enzymes, which belongs to Block X of the α/β-hydrolase enzymes classified in the ESTHER database [2]. This family includes fungal and bacterial tannases and feruloylesterases. Other significantly different bacterial tannases can be found in a separate H block (Tannases_bact) in this database. Accordingly, MHETase has been shown to hydrolyze exclusively MHET but not BHET, PET, p-nitrophenyl (pNP) aliphatic esters or aromatic ester compounds such as ethyl gallate and ethylferulate, which are converted by other enzymes in the tannase family, indicating a severely limited substrate specificity [3].

Functional annotation of the enzyme MHETase was performed using the InterPro program. Figure 1 shows the annotation of the MHETase enzyme.

Figure 1 - Functional annotation of the MNETase enzyme.

The InterPro and Panter databases classify the enzyme MHETase as a tannase and feruloylesterase family and provide the following description: this family includes fungal tannases [4] and feruloylesterases [5, 6]. It also includes mono(2-hydroxyethyl) terephthalate hydrolase from the bacterium Ideonella sakaiensis [7] and several bacterial homologs with unknown function.

The Pfam database provides information on the relationship of the enzyme to the tannase and feruloylesterase family and provides the following description: this family includes fungal tannases [4, p. 217] and feruloylesterase [5, p. 381., 6, p. 258]. It also includes several bacterial homologs with unknown function.

The InterPro protein homologous superfamily refers as well as the PETase enzyme to alpha/beta hydrolase.

All plastic-degrading enzymes known to date have an α/β-hydrolase fold. However, MHETase probably possesses an unprecedented framework for plastic degrading enzymes.

Structural comparison of MHETase from Ideonella sakaiensis and feruloylesterase FaeB from Aspergillus oryzae

The overall architecture of the 65 kDa domain of MHETase resembles that of feruloylesterase, with a leader domain embedded between β-chain 7 and α-helix 15 of the α/β-hydrolase fold [8]. As previously observed for feruloylesterase, the presence of a structural calcium binding site was confirmed by X-ray fluorescence spectroscopy for MHETase. Similarly, one of the five disulfide bonds flanks the catalytic triad (formed by S225, H528, D492) and an oxyanion hole containing the nitrogen atoms of the main chain amide of G132 and E226. In the ligand-free structure of MHETase, several water molecules are retained by a hydrogen bond network at the substrate binding site. While the α/β-hydrolase domain overlaps well with the closest structurally characterized homolog of feruloylesterase FaeB from Aspergillus oryzae (1.60 Å RMSD for aligned 280 of 342 residues, 32.5% amino acid identity), the closing domain of MHETase contains several additional loops that differ markedly from FaeB (2.33 Å RMSD for 148 of 215 aligned residues, 18.9% identity). The overall structures of MHETase and FaeB are structurally similar (2.04 Å RMSD for 421 of 559 aligned residues) despite relatively few amino acid identities (27.5%). When comparing MHETase with known tannase structures, such as tanninacyl-α/β-hydrolase from Lactobacillus plantarum (LptE), it becomes apparent that only the common fold of the α/β-hydrolase domain is similar (2.77 Å RMSD for 195 of 282 residues aligned, identity 13.8). PETase and MHETase share a common fold only α/β-hydrolase domain (2.87 Å RMSD for 184 of 262 residues aligned) [8, p. 1720].

Structure of MHETase bound to a non-hydrolyzable ligand

The main chain conformation in the structure of the MHETase-MHETA complex is almost identical to that of MHETase without substrate (RMSD 0.54 Å) and sheds light on the position of MHET for catalysis. Although the catalytic triad and oxyanion hole residues are part of the α/β-hydrolase domain, substrate specificity is almost exclusively provided by the cap domain. Hydrophobic contacts between the phenyl ring of MHETA and the α/β-hydrolase domain are restricted predominantly to F495 and to a lesser extent to G132 and A494. Surprisingly, MHETA is firmly bound by the closing domain residues F415, L254 and W397 surrounding almost the entire phenyl fragment of MHETA. Two oxygen atoms of the free carboxylate make contact with R411, which is held by S416, S419 and the main chain amide G258, which maintain a hydrogen bonding network involving three water molecules [8, p. 1720].

Despite their overall high similarity, a detailed comparison of MHETase structures in the absence and presence of substrate reveals a mechanism of induced compliance upon MHETA binding. In the ligand-free structure, F415 is directed away from the active center and thus opens it for substrate binding [8, p. 1720].

Unlike PETase, MHETase binds very strongly to its substrate. The position of the substrate in the active center of MHETase resembles tanninacyl α/β-hydrolase from Lactobacillus plantarum bound to ethyl gallate (LptE), but shows marked differences with respect to residues contacting the substrate at the interface. [8, p. 1721].

3D structure of MNETase enzyme

Using the SWISS-MODEL program, the 3-D structure of the MNETase enzyme was constructed, its structure is shown in Figure 2.

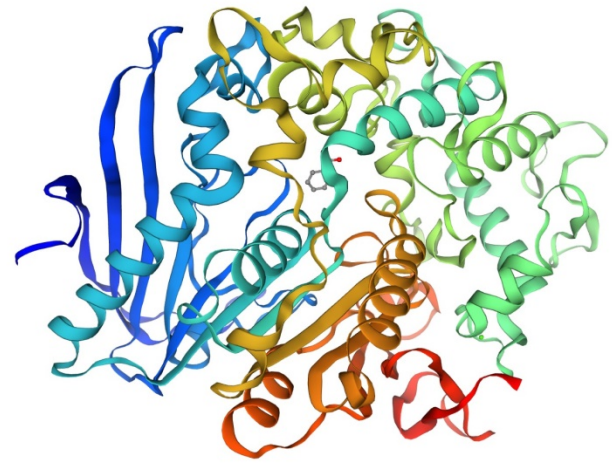


Figure 2 - 3D structure of the MHETase enzyme.

The 3D structure of the enzyme MNETase revealed the crystal structure of PETase S121D, mutant D186H from Ideonella sakaiensis, in the range of amino acids 417-518. This may indicate similar functions of these enzymes.

References

1. Knott B.C., Erickson E., Allen M.D., Gado J.E., Graham R., Kearns F.L., Pardo I., Topuzlu E., Anderson J.J., Austin H.P., Dominick G., Johnson C.W., Rorrer N.A., Szostkiewicz C.J., Copié V., Payne C.M., Woodcock H.L., Donohoe B.S., Beckham G.T., McGeehan J.E. Characterization and engineering of a two-enzyme system for plastics depolymerization // Proc Natl Acad Sci U S A. – 2020. – Vol. 117, № 41. – P. 25476-25485.

2. Lenfant N., Hotelier T., Velluet E., Bourne Y., Marchot P., Chatonnet A. ESTHER, the database of the α/β-hydrolase fold superfamily of proteins: tools to explore diversity of functions // Nucleic Acids Res. – 2013. – Vol. 41. – P. 423-429.

3. Yoshida S., Hiraga K., Takehana T., Taniguchi I., Yamaji H., Maeda Y., Toyohara K., Miyamoto K., Kimura Y., Oda K. A bacterium that degrades and assimilates poly(ethylene terephthalate) // Science. – 2016. – Vol. 351. – P. 1196–1199.

4. Hatamoto O, Watarai T, Kikuchi M, Mizusawa K, Sekine H. Cloning and sequencing of the gene encoding tannase and a structural study of the tannase subunit from Aspergillus oryzae // Gene. - 1996. - Vol. 175. – P. 215-221.

5. Vries RP, vanKuyk PA, Kester HC, Visser J. The Aspergillus niger faeB gene encodes a second feruloyl esterase involved in pectin and xylan degradation and is specifically induced in the presence of aromatic compounds // Biochem. J. – 2002. – Vol. 363. – P. 377-386.

6. Kroon PA, Faulds CB, Williamson G. Purification and characterization of a novel esterase induced by growth of Aspergillus niger on sugar-beet pulp // Biotechnol. Appl. Biochem. – 1996. – Vol. 23, № 3. – P. 255-262.

7. Yoshida S, Hiraga K, Takehana T, Taniguchi I, Yamaji H, Maeda Y, Toyohara K, Miyamoto K, Kimura Y, Oda K. A bacterium that degrades and assimilates poly(ethylene terephthalate) // Science. – 2016. – Vol. 351. – P. 1196-1199.

8. Palm G.J,, Reisky L., Böttcher D., Müller H., Michels E., Walczak M.C., Berndt L., Weiss M.S., Bornscheuer U.T., Webercorresponding G. Structure of the plastic-degrading Ideonella sakaiensis MHETase bound to a substrate // Nat Commun. – 2019. – Vol. 10. – P. 1717-1727.

УДК: 616-006.699

Применение peg-plga наночастиц для терапии колоректального рака

Махамбетова Айгерим Муратовна[1, 2]
[1]Евразийский национальный университет им. Л. Н. Гумилева, 010008,
Республика Казахстан, г. Астана, ул. Кажымукан 13,
[2]Частное учреждение «National Laboratory Astana», 010000, Республика Казахстан,
г.Астана, пр. Кабанбай батыра 53
Научный руководитель – А.Ж. Бектурова[1]
Со-руководитель – Б.А. Умбаев[2]
aika92604@gmail.com

Колоректальный рак представляет собой серьезную проблему общественного здравоохранения, стоящую на втором месте среди всех типов злокачественных опухолей и занимающую четвертое место по смертности от рака в мире. Согласно данным Американского онкологического общества на 2020 год, в США было зарегистрировано 104 610 новых случаев рака толстой кишки и 43 340 новых случаев рака прямой кишки. Риск заболевания колоректального рака в течение жизни оценивается примерно 1 случай на 23 для мужчин и 1 случай на 25 для женщин [1].

Лечение рака всегда было областью больших исследований из-за сложных и обширных вариантов лечения, а также серьезных побочных эффектов химиотерапевтических препаратов. Существует множество противораковых препаратов, доступных для использования, но их терапевтическое значение ограничено такими факторами, как плохая растворимость, низкая абсорбция и множественная лекарственная устойчивость [2]. В последние годы чрезвычайно интригующим предметом для изучения стало использование нанотехнологий, то есть использования наночастиц в качестве инструмента доставки лекарств для лечения и диагностики заболеваний [3]. Среди всех других применений их использование в качестве стратегических средств лечения рака имеет особое значение. В этом обзоре показаны свойства наночастиц PEG-PLGA, а также их применение в качестве систем доставки лекарств, нацеленных конкретно на колоректальный рак.

Наночастицы представляют собой твердые сферические везикулы размером от 1 до 100 нанометров. Биосовместимые и биоразлагаемые полимеры были разработаны с использованием природных и синтетических материалов, но синтетические наночастицы более желательны для терапевтического использования, поскольку их можно модифицировать для достижения желаемых свойств, необходимых для контролируемого и целевого высвобождения лекарств. Одним из таких известных синтетических материалов является PLGA - сополимер полимолочной и гликолевой кислот. Полимер PLGA обладает превосходными свойствами управляемого и целенаправленного распределения в толстой кишке вместе с лекарственными препаратами, благодаря чему он обеспечивает интеллектуальную деградацию в организме. Его способность к разложению контролируется числом гликолидных единиц: снижение концентрации гликоля способствует улучшению разложения, в то время как повышение этой концентрации имеет противоположный эффект [4]. Кроме того, PLGA эффективно способствует доставке лекарственных средств при колоректальном раке, повышая их эффективность, обеспечивая оптимальный профиль медленного высвобождения, увеличивая