

Title of the project:	
<u>U</u>rinary <u>T</u>ract <u>I</u>nfection and <u>L</u>evels of heat shock protein 70 <u>I</u>n children as a <u>S</u>ensitive marker for <u>E</u>xcluding other infections (UTILISE)	
Principal investigator	Year of award
Alev YILMAZ	2018
Please provide an overall summary of the project (max 500 words)	
The World Health Organization declared antimicrobial resistance one of the top ten threats to global public health. Avoiding unnecessary antibiotic therapies is a key strategy to limit bacterial resistance. In children, suspected urinary tract infection (UTI) is one of the most common causes of empiric antibiotic therapy since the definitive diagnosis depends on urine culture results which are obtained with 24-48 hour delay. The majority of these patients would not need antibiotic treatment. Saha et al. reported that urine culture did not confirm the diagnosis in 84% of patients who received empiric antibiotic therapy for presumed UTI. Pediatricians often struggle with making the diagnosis of UTI because of the non-specificity of symptoms especially in infants, frequent contamination of urine samples, occasional non-invasive bacterial colonization of the bladder and, most importantly, the limited specificity of conventional urinalysis by leukocyte microscopy and dipstick biochemical testing. Hence, there is a need for more sensitive and specific diagnostic biomarkers of UTI that can help minimizing the number of unnecessary antibiotic therapies. Heat Shock Protein 70 (HSP70) is a member of the Heat Shock Protein family which are synthesized in response to hazardous factors, including infections, to protect the protein structure of the cells. HSP70 is released from macrophages exposed to bacterial products, especially Gram-negative bacteria such as <i>Escherichia coli</i> (<i>E. coli</i>). HSP70 is also secreted by tubuloepithelial cells under stress conditions. Our aim was to find a fast and easy way for accurate diagnosis of UTI while urine culture is pending. We planned UTILISE Study, a large multicenter study specifically designed to determine if urine and/or serum HSP70 level, TLRs and antimicrobial peptides as a diagnostic biomarker distinguishing UTI from other infections and conditions.	
How was the grant used for the project? (max 200 words)	

The kits used for laboratory tests were purchased with this grant.

Please list all publications completed, with links to open access publications where available

1. Yilmaz A, Afonso AC, Akil I, Aksu B, Alpay H, Atmis B, Aydog O, Bayazit AK, Bayram MT, Bilge I, Bulut IK, Buyukkaragoz B, Comak E, Demir BK, Dincel N, Donmez O, Durmus MA, Dursun H, Dusunsel R, Duzova A, Ertan P, Gedikbasi A, Goknar N, Guven S, Hacıhamdioglu D, Jankauskiene A, Kalyoncu M, Kavukcu S, Kenan BU, Kucuk N, Kural B, Litwin M, Montini G, Morello W, Nayir A, Obrycki L, Omer B, Ozdemir EM, Ozkayin N, Paripovic D, Pehlivanoglu C, Saygili S, Schaefer S, Sonmez F, Tabel Y, Tas N, Tasdemir M, Teixeira A, Tekcan D, Tulpar S, Turkkan ON, Uysal B, Uysalol M, Vaiciuniene D, Yavuz S, Yel S, Yildirim T, Yildirim ZY, Yildiz N, Yuksel S, Yurtseven E, Schaefer F, Topaloglu R. Urinary HSP70 improves diagnostic accuracy for urinary tract infection in children: UTILISE study. *Pediatr Nephrol*. 2023 Mar;38(3):791-799. (<https://pubmed.ncbi.nlm.nih.gov/35849222/>).
2. Aksu B, Afonso AC, Akil I, Alpay H, Atmis B, Aydog O, Bayazit AK, Bayram MT, Bilge I, Bulut IK, Buyukkaragoz B, Comak E, Demir BK, Dincel N, Donmez O, Durmus MA, Dursun H, Dusunsel R, Duzova A, Ertan P, Gedikbasi A, Goknar N, Guven S, Hacıhamdioglu D, Jankauskiene A, Kalyoncu M, Kavukcu S, Kenan BU, Kucuk N, Kural B, Litwin M, Montini G, Morello W, Obrycki L, Omer B, Oner HA, Ozdemir EM, Ozkayin N, Paripovic D, Pehlivanoglu C, Saygili S, Schaefer F, Schaefer S, Sonmez F, Tabel Y, Tas N, Tasdemir M, Teixeira A, Tekcan D, Topaloglu R, Tulpar S, Turkkan ON, Uysal B, Uysalol M, Vitkevic R, Yavuz S, Yel S, Yildirim T, Yildirim ZY, Yildiz N, Yuksel S, Yurtseven E, Yilmaz A. Urine soluble TLR4 levels may contribute to predict urinary tract infection in children: the UTILISE Study. *Pediatr Nephrol*. 2024 Feb;39(2):483-491. (<https://pubmed.ncbi.nlm.nih.gov/37462743/>).
3. Aksu B, Afonso AC, Akil I, Alpay H, Atmis B, Aydog O, Bakkaloglu S, Bayazit AK, Bayram MT, Bilge I, Bulut IK, Cetinkaya APG, Comak E, Demir BK, Dincel N, Donmez O, Durmus MA, Dursun H, Dusunsel R, Duzova A, Ertan P, Gedikbasi A, Goknar N, Guven S, Hacıhamdioglu D, Jankauskiene A, Kalyoncu M, Kavukcu S, Kenan BU, Kucuk N, Kural B, Litwin M, Montini G, Morello W, Obrycki L, Omer B, Misirli Ozdemir E, Ozkayin N, Paripovic D, Pehlivanoglu C, Saygili S, Schaefer F, Schaefer S, Sonmez F, Tabel Y, Tas N, Tasdemir M, Teixeira A, Tekcan D, Topaloglu R, Tulpar S, Turkkan ON, Uysal B, Uysalol M, Vitkevic R, Yavuz S, Yel S, Yildirim T, Yildirim ZY, Yildiz N, Yuksel S, Yurtseven E, Yilmaz A. The relationship between urine heat shock protein 70 and congenital anomalies of the kidney and urinary tract: UTILISE study. *Front Urol*. 2024 Feb 28;3:1281081. (<https://pubmed.ncbi.nlm.nih.gov/40778050/>).

Are any other publications planned?

We have two manuscripts under peer review, one in Pediatric Nephrology and the other in BMJ Infectious Disease.

Another manuscript is being prepared.

Please list all presentations relating to the project

1. Yildirim Yuruk Zeynep Nagehan, **Aksu Bagdagul**, Afonso Alberto Caldas, Akil Ipek, Alpay Harika, Atmiş Bahriye, Aydog Ozlem, Bakkaloglu Sevcan, Karabay Bayazit Aysun, Torun Bayram Meral, Bilge IImay, Kaplan Bulut Ipek, Comak Elif, Delebe Cam Ozlem, Demir Kasap Belde, Dincel Nida, Donmez Osman, Durmus Mehmet Akif, Dursun Hasan, Dusunsel Ruhan, Duzova Ali, Ertan Pelin, Gedikbaşı Asuman, Goknar Nilufer, Guven Sercin, Hacıhamdioglu Duygu, Jankauskiene Augustina, Kalyoncu Mukaddes, Kavukcu Salih, Kenan Uzun Bahriye, Kucuk Nuran, Kural Bahar, Litwin Mieczslaw, Montini Giovanni, Morello William, Obrycki Lukasz, Omer Beyhan, Ozdemir Misirli Ebru, Ozkayin Emine Nese, Paripovic Dusan, Pehlivanoglu Cemile, Saygili Seha, Schaefer Franz, Schaefer Susanne, Sonmez Ferah, Tabel Yilmaz, Tas Nesrin, Tasdemir Mehmet, Teixeira Ana, Tekcan Karali Demet, Topaloglu Rezan, Tulpar Sebahat, Turkkan Ozde Nisa, Uysal Berfin, Uysalol Metin, Daiva Vaiciuniene, Yavuz Sevgi, Yel Sibel, Yildirim Tarik, Yildiz Nurdan, Yuksel Selcuk, Yurtseven Eray, Yilmaz Alev. "The Role of Antimicrobial Polypeptides for the Predicting of Urinary Tract Infection: UTILISE Study", ESPN 55th Annual Meeting 28 September-1 October 2023, Vilnius, Lithuania

2. Yilmaz Alev, Afonso Alberto Caldas, Akil Ipek, **Aksu Bagdagul**, Alpay Harika, Atmış Bahriye, Aydog Ozlem, Karabay Bayazit Aysun, Torun Bayram Meral, Bilge IImay, Kaplan Bulut Ipek, Buyukkaragoz Bahar, Comak Elif, Demir Kasap Belde, Dincel Nida, Donmez Osman, Durmus Mehmet Akif, Dursun Hasan, Dusunsel Ruhan, Duzova Ali, Ertan Pelin, Gedikbaşı Asuman, Goknar Nilufer, Guven Sercin, Hacıhamdioglu Duygu, Jankauskiene Augustina, Kalyoncu Mukaddes, Kavukcu Salih, Kenan Uzun Bahriye, Kucuk Nuran, Kural Bahar, Litwin Mieczslaw, Montini Giovanni, Morello William, Nayir Nevzat Ahmet, Obrycki Lukasz, Omer Beyhan, Ozdemir Misirli Ebru, Ozkayin Emine Nese, Paripovic Dusan, Pehlivanoglu Cemile, Saygili Seha, Schaefer Susanne, Sonmez Ferah, Tabel Yilmaz, Tas Nesrin, Tasdemir Mehmet, Teixeira Ana, Tekcan Karali Demet, Tulpar Sebahat, Turkkan Ozde Nisa, Uysal Berfin, Uysalol Metin, Vaiciuniene Daiva, Yavuz Sevgi, Yel Sibel, Yildirim Tarik, Yildirim Yuruk Zeynep Nagehan, Yildiz Nurdan, Yuksel Selcuk, Yurtseven Eray, Schaefer Franz, Topaloglu Rezan, Urinary HSP70 improves diagnostic accuracy for urinary tract infection in children: UTILISE study. *Pediatric Nephrology* 2023;38:791–799
3. **Aksu Bagdagul**, Afonso Alberto Caldas, Akil Ipek, Alpay Harika, Atmış Bahriye, Aydog Ozlem, Karabay Bayazit Aysun, Torun Bayram Meral, Bilge IImay, Kaplan Bulut Ipek, Buyukkaragoz Bahar, Comak Elif, Demir Kasap Belde, Dincel Nida, Donmez Osman, Durmus Mehmet Akif, Dursun Hasan, Dusunsel Ruhan, Duzova Ali, Ertan Pelin, Gedikbaşı Asuman, Goknar Nilufer, Guven Sercin, Hacıhamdioglu Duygu, Jankauskiene Augustina, Kalyoncu Mukaddes, Kavukcu Salih, Kenan Uzun Bahriye, Kucuk Nuran, Kural Bahar, Litwin Mieczslaw, Montini Giovanni, Morello William, Obrycki Lukasz, Omer Beyhan, Oner Huseyin Adil, Ozdemir Misirli Ebru, Ozkayin Emine Nese, Paripovic Dusan, Pehlivanoglu Cemile, Saygili Seha, Schaefer Franz, Schaefer Susanne, Sonmez Ferah, Tabel Yilmaz, Tas Nesrin, Tasdemir Mehmet, Teixeira Ana, Tekcan Karali Demet, Topaloglu Rezan, Tulpar Sebahat, Turkkan Ozde Nisa, Uysal Berfin, Uysalol Metin, Vitkevic Renata, Yavuz Sevgi, Yel Sibel, Yildirim Tarik, Yildirim Yuruk Zeynep Nagehan, Yildiz Nurdan, Yuksel Selcuk, Yurtseven Eray, Yilmaz Alev. Urine soluble TLR4 levels may contribute to predict urinary tract infection in children: the UTILISE Study. *Pediatric Nephrology* 2024;39:483–491
4. **Bagdagul Aksu**, Afonso Alberto Caldas, Akil Ipek, Alpay Harika, Atmış Bahriye, Aydog Ozlem, Bakkaloglu Sevcin, Karabay Bayazit Aysun, Torun Bayram Meral, Bilge IImay, Kaplan Bulut Ipek, Cetinkaya Goksu Ayse Pinar, Comak Elif, Demir Kasap Belde, Dincel Nida, Donmez Osman, Durmus Mehmet Akif, Dursun Hasan, Dusunsel Ruhan, Duzova Ali, Ertan Pelin, Gedikbaşı Asuman, Goknar Nilufer, Guven Sercin, Hacıhamdioglu Duygu, Jankauskiene Augustina, Kalyoncu Mukaddes, Kavukcu Salih, Kenan Uzun Bahriye, Kucuk Nuran, Kural Bahar, Litwin Mieczslaw, Montini Giovanni, Morello William, Obrycki Lukasz, Omer Beyhan, Ozdemir Misirli Ebru, Ozkayin Emine Nese, Paripovic Dusan, Pehlivanoglu Cemile, Saygili Seha, Schaefer Franz, Schaefer Susanne, Sonmez Ferah, Tabel Yilmaz, Tas Nesrin, Tasdemir Mehmet, Teixeira Ana, Tekcan Karali Demet, Topaloglu Rezan, Tulpar Sebahat, Turkkan Ozde Nisa, Uysal Berfin, Uysalol Metin, Vitkevic Renata, Yavuz Sevgi, Yel Sibel, Yildirim Tarik, Yildirim Yuruk Zeynep Nagehan, Yildiz Nurdan, Yuksel Selcuk, Yurtseven Eray, Yilmaz Alev. The relationship between urine heat shock protein 70 and congenital anomalies of the kidney and urinary tract: UTILISE study. *Front. Urol* 2024:1-7