UNIQUE ASPECTS OF THE HYPERTHERMOPHILE PROTEOME

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Summary

Comparison of 52 complete genome sequences from hyperthermophilic and nonhyperthermophilic archaea and bacteria show that at least 10% of the open reading frames (ORFs) in archaea are conserved within this domain and not found in either the bacteria or eukaryotes. Unfortunately, the function of these ORFs is largely unknown and so purification and characterization of the encoded proteins, coupled with functional genomic approaches involving proteomics and DNA microarrays, are clearly needed to identify the archaeal 'core' genes. One of the most thoroughly studied orders of archaea is the Thermococcales, which is composed of the *Pyrococcus* and *Thermococcus* genera. These organisms grow optimally above 80 °C and thus are hyperthermophiles. A total of 135 proteins, either native or recombinant, have been characterized from the Thermococcales, primarily from *P. furiosus* and *T.*

kodakaraensis. Approximately 15% of these proteins are unique to either hyperthermophiles or archaea. The properties of several of these proteins have allowed metabolic pathways to be predicted. For example, based on the characteristics of purified proteins, starch degradation is proposed to involve 27 different steps in *P. furiosus*. Of these, proteins that catalyze 22 of the steps have been purified, and 7 of their sequences are found only in hyperthermophiles or in archaea. The other proteins that have been characterized from the Thermococcales are involved in utilizing other carbohydrates, peptide hydrolysis and catabolism, macromolecule biosynthesis, DNA replication and repair, gene regulation, and oxygen detoxification. The complete genome sequences of three *Pyrococcus* species (*P. abyssi*, *P. furiosus*, and *P. horikoshii*) are available and about half of the approximately 2000 ORFs that each contains encode proteins of completely unknown function. Further insight into function might be provided by the three-dimensional structures of such proteins, for example, as they become available through structural genomic initiatives using either *P. furiosus* or homologous proteins from other organisms.

1. Introduction

Hyperthermophilic microorganisms were first described in 1981 and as such are quite recent additions to the field of microbiology. Their ability to grow at high temperatures in geothermal ecosystems devoid of sunlight and their potentially ancient life history has made them appealing subjects of study for industrialists, astrobiologists, and natural historians, as well as microbiologists and biochemists. One of the key questions is: how do these organisms thrive at temperatures that are lethal to all other life? Potential mechanisms by which nucleic acids, lipids, and other biological molecules are stabilized under hyperthermophilic conditions are reviewed in other chapters within this volume.

The advent of genomic sequencing allows for the comparison of the complete genomic compliments of various organisms. The complete genome sequences from eight hyperthermophiles (six archaea and two bacteria) are available (the Comprehensive Microbial Genome Resource, <www.tigr.org>). The ORFs from these genomes plus those from the genomes of 44 other bacteria and archaea were divided into known (i.e., characterized and/or significantly homologous to characterized ORFs in other organisms), conserved hypothetical (i.e., of unknown function but homologs are found in other organisms) and unknown categories. These were compared and the results are shown in Table 1. The percentages for each category among the hyperthermophilic archaea were generally the same as that for all archaea. Likewise, the composition for hypethermophilic bacteria was the same as that for all bacteria. However, the compositions varied between archaea and bacteria. Each contained the same percentage of unknown ORFs, but the average percentage of known ORFs was higher in bacteria while the percentage of conserved hypothetical ORFs was higher in archaea. Even if many of these conserved hypothetical archaeal ORFs are also found in bacteria, there would still be ~10% of these conserved ORFs with unknown function that are either unique to archaea or share homology with eukaryotic ORFs. Four archaeal genomes (i.e., *Methanobacterium thermoautotrophicum*, *Methanococcus jannaschii*, *Archaeoglobus fulgidus*, and *Pyrococcus horikoshii*) were compared and 543 orthologous sets of ORFs (31–35% of the genome) were present in all four species. ORFs related to transcription, translation and DNA replication were most homologous

to eukaryotic ORFs while “housekeeping” ORFs were most homologous to bacterial ORFs. However, there are at least 71 conserved orthologous ORFs that are unique to all four archaea. Therefore, the conclusion from these data is that there are ORFs that are unique to archaea whose functions are largely unknown. Clearly, their characteristics need to be determined through the purification and biochemical analyses of the corresponding proteins.

Herein we focus on the most fundamental aspects of life under extreme conditions, namely, the properties of proteins from hyperthermophiles. Some of those characterized so far are unique to either hyperthermophilic organisms or to archaea at functional or sequence levels, while the others are high-temperature versions of proteins found in many other life forms. Both types are clearly relevant to understanding how organisms can thrive under high temperature conditions. There are 31 genera of hyperthermophiles, three of which are classified as Bacteria and 28 as Archaea. The most thoroughly studied of all of these organisms belongs to the order termed Thermococcales, which consists of the *Pyrococcus* and *Thermococcus* genera. Over 100 different enzymes have been characterized from various species within this order. These have shed some light on the question of biological specialization for high temperature growth, as well as issues related to physiology and metabolism. This chapter will review those proteins that have been purified and characterized from *Pyrococcus* and *Thermococcus* species and examine new methods for determining the function of unknown proteins.

Category	**Known (% ± 1 SD)**	**Conserved hypothetical (% ± 1 SD)**	**Unknown (% ± 1 SD)**	***n***
Hyperthermophilic Archaea	36.6 ± 7.4	32.7 ± 7.2	30.7 ± 12.5	6
Hyperthermophilic Bacteria	49.3 ± 7.3	22.5 ± 1.6	28.2 ± 5.8	2
Non-hyperthermophilic Archaea	39.2 ± 6.7	20.9 ± 7.2	39.9 ± 9.3	5
Non-hyperthermophilic Bacteria	52.8 ± 13.4	17.6 ± 7.9	29.6 ± 15.1	39
All Hyperthermophiles	39.8 ± 9.0	30.1 ± 7.7	30.1 ± 10.9	8
All Nonhyperthermophiles	51.3 ± 13.5	18.0 ± 7.8	30.7 ± 14.8	44
All Archaea	37.8 ± 6.9	27.3 ± 9.2	34.9 ± 11.7	11
All Bacteria	52.6 ± 13.1	17.9 ± 7.9	29.5 ± 14.8	41

Table 1. Percentages of "known," conserved, hypothetical and unknown open-reading frames in hyperthermophilic and nonhyperthermophilic Archaea and Bacteria (error represents one standard deviation)

2. Systematics of the Order Thermococcales

2.1. Phylogeny

All life falls into one of three Domains: the Archaea, the Bacteria, and the Eukarya (or Eukaryotes). The three domains can be differentiated based on features that include the presence of a nucleus, muramic acid in the membranes, lipid chemistry, ribosome size, the presence of introns, RNA polymerase structure, sensitivity to certain antibiotics, and nucleotide sequences of rRNAs. However, the most common and widely accepted

method for the taxonomic classification of bacteria and archaea involves direct comparisons of 16S rRNA nucleotide sequences to form a phylogenetic tree. Most hyperthermophiles are found within the Archaea, and these are further divided into the Crenarchaeota and the Euryarchaeota. Known Crenarchaeotes consist exclusively of thermophilic and hyperthermophilic orders, while the Euryarchaeota include these plus all orders of methanogens and extreme halophiles. The Thermococcales are branched deep among the Euryarchaeota. So far the Thermococcales consist of just two genera: *Pyrococcus* and *Thermococcus.* There are over 10 species of *Pyrococcus* and the complete sequences are known for the genomes of three of them: *P. abyssi, P. furiosus*, and *P. horikoshii*. *Pyrococcus* is the only archaeal genus with complete genome sequences for three or more species. There are over 30 species of *Thermococcus* that have been studied, the highest number of species for any hyperthermophilic genus.

2.2. Growth Characteristics

Species of *Pyrococcus* and *Thermococcus* are all heterotrophic and strictly anaerobic. They all utilize peptides as sources of carbon and energy, and significant growth of virtually all species requires elemental sulfur (S°). The exceptions are *P. furiosus, P. woesei, P. glycovorans*, and *T. litoralis*, as these are capable of growth using carbohydrates as carbon and energy sources when trace amounts of certain peptides and vitamins are provided in the medium, and this growth is independent of S° utilization. The major metabolic products for those strains growing without S° are H_2, CO_2, and acetate. Alanine is produced in lieu of acetate and H_2 when the partial pressure of H_2 becomes inhibitory for growth. These products plus H_2S are formed when all Thermococcales are grown with S°. The key distinction between species classified as either *Pyrococcus* or *Thermococcus* is their temperature range for growth. Species of *Pyrococcus* generally grow between 65 and 105 °C with an optimum growth temperature near 100 °C while *Thermococcus* species grow between 50 and 93 °C with an optimum around 85 °C. All Thermococcales are marine organisms that grow at near neutral pH, except for *T. alcaliphilus* which grows optimally near pH 9 and *T. waiotapuensis* and *T. zilligii* which grow in fresh water.

2.3. Habitats

The first species of Thermococcales known (*T. celer, P. furiosus*, and *P. woesei*) were isolated from shallow marine hot seeps along the coast of Italy. Most other *Pyrococcus* and *Thermococcus* species have been isolated from deep-sea hydrothermal vent environments in the Atlantic and Pacific Oceans. Within these environments, species of *Pyrococcus* and *Thermococcus* have been isolated from vent polychaete worms that live on the outer surface of black smoker chimneys, from within sulfide deposits emitting hydrothermal fluids up to 400 °C, and from low-temperature hydrothermal fluids from subseafloor sources. Other *Thermococcus* spp. have been detected in crude oil extracted from marine oil reservoirs. So far, all *Pyrococcus* species have been discovered in marine environments, but two *Thermococcus* species, *T. waiotapuensis* and *T. zilligii*, have been isolated from freshwater ecosystems, in both cases from thermal pools in New Zealand.

3. Characterized Enzymes and Proteins

There are 135 enzymes and proteins that have been at least partially characterized from species of *Pyrococcus* and *Thermococcus*. Of these, 114 are close relatives or orthologs of proteins that have been purified from organisms that are not hyperthermophiles or archaea (Table 2). The remaining 21 proteins have properties that are unique to either hyperthermophiles or archaea or both (Table 3). The 114 orthologous proteins that have been purified come from 17 species of *Thermococcus* and 9 of *Pyrococcus*. Most are from *P. furiosus* (59%), with the remainder from *T. kodakaraensis* (25%), *T. litoralis* (15%), *P. woesei* (11%), *P. horikoshii* (11%), and *P. abyssi* (7%). Less than half (41%) of these proteins have been purified from the native organism, and recombinant versions are also available for more than half of these (24% of total). The other proteins (59%) have been obtained using recombinant techniques only and the native versions have not been characterized. Those proteins with features unique to hyperthermophiles and archaea are primarily from *P. furiosus* (76%). They have been obtained in their native (28%) or recombinant (48%) forms or as both (24%). In the following we have classified the various proteins that are available and briefly describe their properties.

Protein Name	EC Number	Organism[a]	Source[b]
Oxidoreductases (EC 1.-.-.-):			
Alcohol dehydrogenase I (ADH)	1.1.1.2	T.AN1,T.ES1, Th,Tl,Pf	N,R
Alcohol dehydrogenase II, short-chain (AdhA)	1.1.1.2	Pf	R
Glyoxylate reductase	1.1.1.26	Tl	N,R
Isocitrate dehydrogenase (IDH)	1.1.1.41	Pf	R
Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)	1.2.1.12	Pw	N,R
Pyruvate ferredoxin oxidoreductase (POR)	1.2.7.1	Pf	N
Glutamate dehydrogenase (GDH)	1.4.1.3	Tk,Tl,Tpr, P.ES4,Pf,Pw	N,R
L-Proline dehydrogenase (ProDH)	1.5.99.8	Tpr	N
NADH oxidase (NOX1)	1.6.99.-	Pf	R
Hydrogenase I	1.12.1.2	Tc,Tl,Ts,Pf	N
Hydrogenase II	1.12.1.2	Pf	N
Superoxide reductase (SOR)	1.15.1.-	Pf	N,R
Ribonucleotide reductase (RNR)	1.17.4.-	Pf	N
Ferredoxin:NADP oxidoreductase (FNOR)	1.18.1.2	Pf	N
NADP:rubredoxin oxidoreductase (NROR)	1.18.1.4	Pf	N
Hydrogenase, membrane-bound	1.18.99.1	Pf	N
Transferases (EC 2.-.-.-):			
tRNA methyltransferase (Trm1)	2.1.1.32	Pf	R
O^6-Methylguanine-DNA methyltransferase (MGMT, O^6-alkalylguanine-DNA alkalyltransferase)	2.1.1.63	Tk,Tl,Pf	R
DNA methyltransferase (PspGI, restriction endonuclease)	2.1.1.73	P.GI-H	R
Aspartate transcarbamylase (ATCase)	2.1.3.2	Pa	N,R
Ornithine carbamoyltransferase (OTCase)	2.1.3.3	Pa,Pf	N,R
Maltodextrin phosphorylase (MalP)	2.4.1.-	Tl	N,R
Cyclomaltodextrin glucanotransferase (CGTase)	2.4.1.19	T.B1001	N
tRNA guanine transglycosylase (TGT)	2.4.2.29	Ph	R
Alanine aminotransferase (AlaAT)	2.6.1.2	Pf	N,R
Aromatic aminotransferase (ArAT)	2.6.1.57	Tl,Tpr,Pf,Ph	N
Glycerol kinase (GlpK)	2.7.1.30	Tk	R

Carbamoyl-phosphate-synthesizing carbamate kinase (CK)	2.7.2.2	Pa,Pf	N,R
3-Phosphoglycerate kinase (3-PGK)	2.7.2.3	Pw	R
DNA primase p41	2.7.7.-	Pf	R
DNA primase p46	2.7.7.-	Pf	R
DNA-dependent RNA polymerase (DNA primase)	2.7.7.6	Pf	R
DNA polymerase I, α-like Family B (PolI)	2.7.7.7	Ta,Tc,Tf,Tg, Tk,Tl,T.9°N-7, Pa,Pf,Ph,Pw	N,R
Phosphoenolpyruvate synthetase (PpsA)	2.7.9.2	Pf	N
Hydrolases (EC 3.-.-.-):			
Endonuclease I	3.1.-.-	Tf,Th,Tk,Tl,Pf	R
Endonuclease II	3.1.-.-	Tf,Tk,Pf	R
Flap endonuclease (FEN-1)	3.1.-.-	Pf,Ph	R
Double-stranded DNA break repair protein (Rad50)	3.1.-.- 3.6.1.8	Pf	R
Double-stranded DNA nuclease (Mre11)	3.1.-.- 3.6.1.8	Pf	R
DNA-dependent ATPase D-loop formation protein (RecA)	3.1.-.- 3.6.1.8	Tk	R
β-carboxyesterase	3.1.1.1	Pa,Pf	R
Phospholipase A(2)	3.1.1.4	Ph	N
Alkaline phosphatase (AP)	3.1.3.1	Pa	R
4-Nitrophenylphosphatase (PNPPase)	3.1.3.41	Pf	N
RNase HII	3.1.26.-	Tk	R
Ribonuclease P (rnpB, ribozyme)	3.1.26.5	Tc	R
Amylopullulanase (Apu)	3.2.1.- 3.2.1.41	Ta,Th,Tl, Pf,Pw	N,R
α-Amylase (AmyA, 4-α-glucotransferase)	3.2.1.1 2.4.1.-	Th,Tk,Tl,Tpr, T.B1001, Pf,Pw	N,R
β-1,4-Endoglucanase (glycosidase family 5)	3.2.1.4	Ph	R
β-1,4-Endoglucanase (EglA)	3.2.1.4	Pf	R
β-1,3-Laminarinase (LamA)	3.2.1.6	Pf	R
Chitinase (ChiA)	3.2.1.14	Tch,Tk	R
α-Glucosidase (sucrose α-glucohydrolase, invertase)	3.2.1.20	Th,Pf	N,R
β-Glucosidase (CelB)	3.2.1.21	Pf	N,R
β-Mannosidase (BmnA, β-galactosidase)	3.2.1.23 3.2.1.25	Pf,Pw	N,R
Cyclomaltodextrinase (CDase)	3.2.1.54	T.B1001	R
β-Glycosidase	3.2.1.120	Tk,Ph	R
Proteinase, thiol	3.4.-.-	Tk	N
Aminopeptidase	3.4.11.-	Ph	R
Deblocking aminopeptidase (DAP)	3.4.11.-	Pf	R
Methionine aminopeptidase (MAP)	3.4.11.18	Pf	N,R
Proline dipeptidase (prolidase)	3.4.13.9	Pf	N,R
Carboxypeptidase (CP)	3.4.17.-	Pf	N
Carboxypeptidase/Aminoacylase (CP/ACY)	3.4.17.- 3.5.1.14	Ph	R
Acylaminoacyl-peptidase (AAP)	3.4.19.1	Ph	R
Pyrrolidone carboxylpeptidase (PCP, pyroglutamyl peptidase I)	3.4.19.3	Tl,Pf	R
Proteinase I, trypsin- and chymotrypsin-like (PfpI)	3.4.21.-	Pa,Pf,Ph	N,R
Proteinase, subtilisin-like (pyrolysin)	3.4.21.-	Tk,Ts,Pf	N

Proteinase, subtilisin-like II	3.4.21.-	Tk	R
Prolyl endopeptidase (PEPase)	3.4.21.26	Pf	R
Aminoacylase (ACY)	3.5.1.14	Pf	N
Cell-division control protein (CdcA)	3.6.1.-	Tk	R
Minichromosome maintenance (MCM) protein	3.6.1.-	Pa	R
Maltose-binding transport ATPase (MalK)	3.6.1.-	Tl	N
Cell-division inhibitor (MinD)	3.6.1.8	Pf	R
DNA-dependent ATPase recombinase (RadA)	3.6.1.8	Pf	R
Replication factor C (RFC)	3.6.1.8	Pf	R
Cell division protein (FtsZ)	3.6.1.15	Tk,Pw	N,R
ATPase, membrane V-type	3.6.1.34	T.KI	N
Lyases (EC 4.-.-.-):			
Ribulose 1,5-bisphosphate carboxylase/oxygenase (rubisco)	4.1.1.39	Tk	N,R
Indole-3-glycerol phosphate synthase (TrpC)	4.1.1.48	Tk	R
Citrate synthase (CS)	4.1.3.7	Pf	R
Anthranilate synthase (TrpEG)	4.1.3.27	Tk	R
Enolase (2-phosphoglycerate hydratase)	4.2.1.11	Pf	N
Tryptophan synthase (TrpAB)	4.2.1.20	Tk,Pf	R
Isomerases (EC 5.-.-.-):			
Peptidyl-prolyl *cis-trans* isomerase (PPIase)	5.2.1.8	T.KS-1	R
Triosephosphate isomerase (TIM)	5.3.1.1	Pw	N,R
Protein disulfide isomerase (PDI, thioltransferase, glutaredoxin)	5.3.4.1	Pf	N,R
Ligases (EC 6.-.-.-):			
Aspartyl tRNA synthetase (AspRS)	6.1.1.12	Tk	R
Glutamine synthetase (GltA)	6.3.1.2	Tk	R
Adenylosuccinate synthetase (PurA)	6.3.4.4	P.ST700	R
DNA ligase (Lig)	6.5.1.1	Tk,Pf	R
Other Proteins:			
Cell division control protein (Cdc6)	-	Pa	R
Cellobiose binding protein (CbtA)	-	Pf	N,R
-Cyclomaltodextrin binding protein (CBP)	-	T.B1001	R
DNA polymerase II-interacting protein (RadB)	-	Pf	R
Ferredoxin (Fd)	-	Tk,Tl,Pf,Pw	N,R
Histone A (HpkA)	-	Tk,P.GB-3a	R
Histone B (HpkB)	-	Tk,Tz	R
Hydrogenase (Ni-Fe) maturation proteins (HypCD)	-	Tl	R
Maltodextrin-binding protein (MBP)	-	Tz,Pf	R
Maltose/trehalose binding protein (MalE)	-	Tl	R
Maltose/trehalose transport proteins (MalFG)	-	Tl	R
Proliferating cell nuclear antigen (PCNA, DNA sliding clamp)	-	Tc,Pf	R
5S rRNA binding protein L18	-	Pf	R
Rubredoxin (Rd)	-	Pf	R
Signal recognition particle 54 (SRP54)	-	Pf	R
Small heat-shock protein (sHSP)	-	T.KS-1,Pf	R
TATA binding protein (TBP)	-	Tc,Tk,Pf,Pw	N,R
TBP-interacting protein (TIP)	-	Tk	N,R
Transcription activator (LrpA)	-	Pf,Ph,Pw	R
Transcription factor IIB (TFIIB)	-	Pf	R

[a]Abbreviations: Ta, *Thermococcus aggregans*; Tc, *T. celer*, Tch, *T. chitonophagus*; Tf, *T. fumicolans*; Tg, *T. gorgonarius*; Th, *T. hydrothermalis*; Tk, *T. kodakaraensis*; Tl, *T. litoralis*; Tpe, *T. peptonophilus*; Tpr,

T. profundus; Ts, *T. stetteri*; Tz, *T. zilligii*; T.AN1, *Thermococcus* sp. strain AN1;T.B1001, *Thermococcus* sp. strain B1001; T.ES1, *Thermococcus* sp. strain ES1; T.KI, *Thermococcus* sp. strain KI; T.KS-1, *Thermococcus* sp. strain KS-1; T. 9°N-7, *Thermococcus* sp. strain 9°N-7; Pa, *Pyrococcus abyssi*; Pf, *P. furiosus*; Ph, *P. horikoshii*; Pw, *P. woesei*; P.ES4, *Pyrococcus* sp. strain ES4; P.GB-3a, *Pyrococcus* sp. strain GB-3a; and P.GI-H, *Pyrococcus* sp. strain GI-H; P.ST700, *Pyrococcus* sp. strain ST700.
[b]Abbreviations: N, native protein; R, recombinant protein.

Table 2. Purified and characterized enzymes and proteins from Pyrococcus and Thermococcus that are homologous to mesophilic enzymes and proteins

Protein Name	EC Number	Organism[a]	Source[b]
Oxidoreductases (EC 1.-.-.-):			
Glyceraldehyde-3-phosphate ferredoxin oxidoreductase (GAPOR)	1.2.7.-	Pf	N
2-Ketoglutarate ferredoxin oxidoreductase (KGOR)	1.2.7.-	Tl	N
2-Ketoisovalerate ferredoxin oxidoreductase (VOR)	1.2.7.-	Tc,T.ES1,Pf, P.ES4	N
Indolepyruvate ferredoxin oxidoreductase (IOR)	1.2.7.-	Tk,Pf	N,R
Aldehyde ferredoxin oxidoreductase (AOR)	1.2.99.3	Pf	N
Formaldehyde ferredoxin oxidoreductase (FOR)	1.2.99.3	Tl,Pf	N
Transferases (EC 2.-.-.-):			
Mannosyl-3-phosphoglycerate synthase (MPGS)	2.4.1.-	Ph	N,R
Glucokinase, ADP-dependent (GLK)	2.7.1.-	Tl,Pf	N,R
Phosphofructokinase, ADP-dependent (PFK)	2.7.1.-	Tz,Pf	N,R
DNA polymerase II (PolII or PolD)	2.7.7.7	Pa,Pf	R
Hydrolases (EC 3.-.-.-):			
Mannosyl-3-phosphoglycerate phosphatase (MPGP)	3.1.3.-	Ph	R
Holliday junction resolvase (Hjc)	3.1.22.4	Pf	R
Chaperonin (thermosome)	3.6.1.8	Tk,T.KS-1,Tl	R
Lyases (EC 4.-.-.-):			
Fructose-1,6-bisphosphate aldolase (FBA)	4.1.2.13	Pf	R
Isomerases (EC 5.-.-.-):			
Glucose-6-phosphate isomerase (PGI, phosphoglucose isomerase)	5.3.1.9	Pf	N,R
Replication initiator protein (Rep75)	5.99.1.-	Pa	R
Reverse gyrase (Rgy)	5.99.1.-	Pf	R
Ligases (EC 6.-.-.-):			
Acetyl-CoA synthetase I (ACSI)	6.2.1.13	Tc,Pf,Pw	N,R
Acetyl-CoA synthetase II (ACSII)	6.2.1.13	Pf	N
Other Proteins:			
Replication protein A41 (RPA41)	-	Pf	R
Replication protein A14 (RPA14)	-	Pf	R
Replication protein A32 (RPA32)	-	Pf	R

[a,b]Refer to Table 2.

Table 3. Purified and characterized proteins from *Pyrococcus* and *Thermococcus* that have functional properties unique to hyperthermophiles or Archaea, or have no homologs in other Domains

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Biographical Sketches

James F. Holden is a post-doctoral research associate in the Department of Biochemistry and Molecular Biology at the University of Georgia. He received BS (1989), MS (1992) and PhD (1996) degrees in Oceanography from the University of Washington in Seattle. His research interests involve the physiological ecology, biochemistry, and geomicrobiology of microorganisms that grow optimally above 80 °C, or hyperthermophiles, and their relationship with deep-sea hydrothermal vents. He has participated in several research cruises to hydrothermal vent sites, which included dives in the deep-sea submarine *Alvin*. His current research is focused on the metabolism of the hyperthermophilic archaeon *Pyrococcus furiosus* using bioinformatics and functional genomics.

Michael W.W. Adams is a Distinguished Research Professor of Biochemistry, Molecular Biology, and Microbiology and codirector of the Center for Metalloenzyme Studies at the University of Georgia. He received BS (1976) and PhD (1979) degrees in Biochemistry from King's College, the University of London, UK. He joined the Biochemistry Department at the University of Georgia as an Assistant Professor in 1987, following six years as a Research and Senior Biochemist at the Corporate Research Laboratories of Exxon Research and Engineering Co. in Annandale, New Jersey, and two years as a postdoctorate research associate at Purdue University. He is currently editor of *Systematic and Applied Microbiology*, *FEMS Microbiology Reviews*, and the *Journal of Bacteriology*. His research interests involve the physiological, biochemical, spectroscopic and structural characterization of a variety of enzymes and proteins involved in the primary metabolic pathways of organisms that grow near 100 °C, the so-called hyperthermophiles, particularly using genome-based approaches. He has edited six books on these topics and is the author of over 220 original publications.